# "COMPARISON OF THE OUTCOME OF DELAYED VERSUS EARLY CLAMPING OF THE UMBILICAL CORD IN PREMATURE NEONATES- A RANDOMISED CONTROLLED TRIAL"

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This is to certify that the dissertation entitled "**COMPARISON OF THE OUTCOME OF DELAYED VERSUS EARLY CLAMPING OF THE UMBILICAL CORD IN PREMATURE NEONATES- A RANDOMISED CONTROLLED TRIAL**" is a bonafide research work done by **REG NO. : BJ0113003.**


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# LIST OF ABBREVIATIONS USED

| | | |
|---|---|---|
| WHO | - | World Health Organization |
| RDS | - | Respiratory Distress Syndrome |
| TTN | - | Transient Tachypnea of Newborn |
| PDA | - | Patent Ductus Arteriosus |
| NEC | - | Necrotizing Enterocolitis |
| AOP | - | Anemia of Prematurity |
| EPO | - | Erythropoietin |
| IVH | - | Intraventricular Haemorrhage |
| ECC | - | Early Cord Clamping |
| ICC | - | Immediate Cord Clamping |
| DCC | - | Delayed Cord clamping |
| PROM | - | Premature Rupture of Membranes |
| ADHD | - | Attention Deficit Hyperactivity Disorder |
| ASD | - | Autism Spectrum Disorder |
| NICU | - | Neonatal Intensive Care Unit |

| | | |
|---|---|---|
| LNMP | - | Last Normal Menstrual period |
| HIV | - | Human Immunodeficiency Virus |
| HbsAg | - | Hepatitis b Surface Antigen |
| CI | - | Confidence Interval |
| RR | - | Relative Risk |
| RCT | - | Randomized Controlled Trail |
| LBW | - | Low Birth Weight |
| VLBW | - | Very Low Birth weight |
| Hct | - | Hematocrit |
| SNAP | - | Score for Neonatal Acute Physiology |
| RBC | - | Red Blood Cell |
| BFV | - | Blood Flow Volume |
| ACOG | - | American College Of Obstetrics and Gynecology |
| RCOG | - | Royal College Of Obstetrics and Gynecology |
| SD | - | Standard deviation |

# ABSTRACT

**Introduction**: Early cord clamping (ECC) has been the usual practice in preterm neonates, predominantly to facilitate immediate resuscitation of the neonate. Delayed cord clamping (DCC) seems to be safe, associated with higher blood volumes, hematocrit, improved hemodynamic stability, lesser incidence of anemia, intraventricular hemorrhage (IVH), need for blood transfusions, without any increase in untoward effects such as lower APGAR scores, polycythemia, jaundice and respiratory distress. Although several studies have shown the beneficial effects of DCC, still there is a lot of anxiety, concern and reluctance among obstetricians to accept this practice. This is primarily due to possible interference with immediate neonatal resuscitation and active management of third stage of labour. Also there is no clear cut consensus regarding the ideal timing of DCC, especially during cesarean section.

**Objective:** To compare the effect of delayed cord clamping ( DCC) versus early cord clamping ( ECC) on hemoglobin levels in gram% on day one of life, peak serum bilirubin levels in mg/dl attained before discharge and on adverse neonatal outcome in late premature neonates, between 34 to 36 weeks 6 days period of gestation.

**Methodology**:

Design: Randomized controlled study.

Setting: KLE University's Dr. Prabhakar Kore Hospital and Medical Research Center, Attached to Jawahar Lal Medical College, Belagavi.

Subjects: 128 pregnant women delivering late premature neonates both vaginally and cesarean sections and fulfilling inclusion criteria, between May 2014 to May 2015 were allocated using computer generated randomization chart.

Intervention: Subjects were randomized into two groups. In DCC (64 subjects), cord was cut after 45 seconds and in ECC (64 subjects), cord was clamped within 5 seconds. Babies delivered vaginally were placed just below the level of the introitus and during cesarean deliveries; babies were placed on sterile drapes between the mother's legs. All babies were gently dried, stimulated, suctioning done if needed. The outcomes assessed were Hb in gm% on Day one of life, highest total and direct serum bilirubin level attained before discharge in mg/dl, APGAR score at 1 and 5 minutes, NICU admission rates, need for phototherapy for hyperbilirubinemia and neonatal mortality rate.

**Results**: The two groups were matched in terms of demographic parameters like maternal age and parity, mechanism of onset of labour, mode of delivery, and indication for induction of labour, indication for LSCS, sex of the neonate, gestational age at delivery and birth weights. Mean hemoglobin levels in gram% on day 1 of life were significantly higher among DCC 15.66 ± 3.12 versus 14.05 ± 3.07 in ECC, $p = 0.0039$. There was no significant difference in mean total serum Bilirubin and mean direct serum bilirubin in (mg/dl) among DCC and ECC (7.92 ± 3.61 versus 8.03 ± 3.18, $p = 0.8552$) and (0.40 ± 0.198 versus 0.371 ± 0.229, $p = 0.449$) respectively. No significant difference was noted in phototherapy (14.10% versus 10.90% $p = 0.592$) and APGAR score at 1 min < 7 (59.37% versus 54.68% $p = 0.592$).

Rate of NICU admission (23.4%) and pregnancy outcome (live birth rates) was same in both groups ($p = 1$).

**Conclusion**: Delayed cord clamping upto 45 secs appears to be a safe and cost effective beneficial tool which significantly improves the hemoglobin levels in late preterm neonates. It does not cause significant risk of hyperbilirubinemia and increased risk of phototherapy, does not compromise the APGAR score at birth. This can be performed during both cesarean and vaginal delivery, with neonates placed at or below the level of introitus. Thus delayed cord clamping in late preterm neonates should be incorporated in routine practice.

**Key words**: Late preterm neonates, Delayed cord clamping, neonatal outcome, hemoglobin levels.

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# INTRODUCTION

A preterm neonate is defined as a baby born alive before 37 completed weeks of gestation by the World Health Organization.[1] A preterm neonate is further sub-classified as extremely preterm (<28.0 weeks gestation), very preterm (28 to <32.0 weeks gestation), moderate preterm (32 to<34.0 weeks gestation) and late preterm (34 to <37.0 weeks gestation).[2, 3]

Worldwide, the frequency of preterm births is estimated to be around 15 millions, with about 41,000 babies born each day. About 5% of these preterm births are extremely preterm.[1] In the United States, the frequency of preterm births is about 12-13% and in many other developed countries it is about 6-9 %.[5] Across 184 countries, the rate of preterm birth ranges from 5% to 18% of babies born.[1] Nearly 24% or one in four children born prematurely across the globe in 2010 were from India. India recorded the highest number of preterm births, at 35.19 lakhs children in 2010. Almost 13% of all children born in India were preterm while China ranked second.[4] Unfortunately, the rate of preterm birth is rising.

In the current scenario, preterm births are predominantly linked to iatrogenic preterm deliveries, artificially conceived multiple pregnancies and advanced maternal age.[5, 6]

Preterm birth is a major global public health issue due to its increasing prevalence, impact upon neonatal mortality and morbidity and high cost implications. Deaths related to prematurity accounted for 35% of all infant deaths in 2010, which is more than any other single cause. It is also the leading cause of long-term neurological disabilities in children.[7]

A broad range of neonatal complications has been documented in the growing body of literature on preterm neonates. These include complications like respiratory distress syndrome (RDS), transient tachypnea of the newborn (TTN), apnoea, patent ductus arteriosus (PDA), hypotension, pulmonary hypertension, intraventricular hemorrhage, hypothermia, poor feeding, necrotizing enterocolitis (NEC), anemia, jaundice, hypoglycaemia and sepsis.[8]

Anemia in a preterm neonate is referred to as anemia of prematurity (AOP), being one of the complications, occurs earlier and is more pronounced in its severity in preterm neonates than the anemia seen in term infants. Erythropoiesis decreases after birth as a result of increased tissue oxygenation due to the onset of breathing and closure of the ductus arteriosus, and a reduced production of erythropoietin (EPO).[9] In term infants, the hemoglobin level typically reaches an average nadir of 11 g/dL at approximately 8 to 12 weeks after birth. This is more predominant in preterm infants who are already born with a lower hematocrit.[9]

Optimizing prenatal, perinatal and post natal care is essential to improve short and long term outcomes of preterm neonates. Despite recent advances in perinatal and neonatal medicine, anemia of prematurity continues to complicate care of these preterm infants, especially those weighing <1,500 kilograms who often require red blood cell transfusions within the first three weeks of life.[10] Although transfusion is the mainstay management for Anemia of prematurity, it is temporary, inhibits erythropoiesis, with risk of infections, graft-versus-host disease and transfusion related lung and gut injuries. Administration of recombinant human erythropoietin, supplementation with iron, folic acid, and vitamin B12 are other strategies to reduce transfusion but all these have unclear benefits and accompanying risks.[11,12,13,14]

The role of umbilical cord clamping on neonatal outcomes in preterm neonates has been a subject of controversy since long. The usual practice in preterm neonates has been early cord clamping, predominantly to facilitate immediate resuscitation of the neonate, and also to prevent post partum hemorrhage as a part of active management of third stage labour.[15]

The timing of umbilical cord clamping after birth has a significant impact on the amount of blood transfused from the placenta to the neonate. During the first 5 to 15 seconds after delivery, blood volume increases by 5 to 15 ml/kg due to uterine contractions. This early placental transfusion does not occur if the cord is clamped immediately or the uterus does not contract.[16] Thus delaying the cord clamping by at least 30 seconds compared to immediate cord clamping results in increased circulating blood volume in the first 24 hours of life, lower incidence of red blood cell transfusion, necrotizing enterocolitis and IVH.[17-26] Delayed cord clamping leads to autologous transfusion of blood from placenta to the neonate of approximately 80 ml. This results in increased hematocrit, blood volume[49,50,19,51,17], increase iron stores, provides more hemopoetic stem cells and more cardiovascular stability, as well as physiologic changes in gastro-intestinal, cardio-pulmonary[52, 53, 54] and renal functions[24] with lesser incidence of anemia, IVH and need for blood transfusions. In preterm low birth weight infants, placental transfusion results in lower incidence of respiratory distress syndrome[55], higher blood volumes and hematocrit, and fewer infants with hypotension.[56] Thus, delayed cord clamping leading to placental transfusions has emerged as a relatively inexpensive and safe intervention that could provide significant benefits like lesser incidence of anemia, IVH and need for blood transfusions.[56,57,20,58,59,60,21]

Because of insufficient studies, it is important to accurately quantitate the increase in neonatal hematocrit indices after delayed umbilical cord clamping before ascribing the possible benefits and adverse findings—or lack thereof—to delayed clamping.

Hence the present study was designed to determine whether delayed cord clamping in preterm neonates would result in a better hematocrit value without increasing the adverse effects and thus a better neonatal outcome, by comparing delayed versus early clamping of umbilical cord in late premature neonates between 34 to 36 weeks 6 days period of gestation.

# AIMS AND OBJECTIVES

The objectives of the present study were:

- To compare the effect of delayed versus early clamping of umbilical cord in late premature neonates between 34 to 36 weeks 6 days period of gestation on haemoglobin levels in gram% on day one of life and peak serum bilirubin levels in mg/dl attained before discharge
- To compare the effect of delayed versus early clamping of umbilical cord in late premature neonates on adverse neonatal outcome

# REVIEW OF LITERATURE

## 3.1 BACKGROUND

Preterm birth is a worldwide serious problem. Complications associated with preterm births is the foremost cause of death among children under five years of age. It is responsible for nearly one million deaths each year. Many survivors face a lifetime of disability, including learning, visual and hearing problems.[1] Also children who are born premature have higher rates of cerebral palsy, sensory deficits, learning disabilities and respiratory illnesses compared with children born at term. The morbidity associated with preterm birth often extends to later life, resulting in enormous physical, psychological and economic costs.[30, 31] Of all early neonatal deaths (deaths within the first 7 days of life) that are not related to congenital malformations, 28% are due to preterm birth.[32]

## 3.2 DEFINITION

Preterm birth is defined as childbirth occurring at less than 37 completed weeks or 259 days of gestation. It is a major determinant of neonatal mortality and morbidity.[27-29]

Delayed cord clamping (DCC) is prolongation of the time between delivery of the baby and clamping the cord. It is performed 25 seconds to 5 minutes after delivery, until cord pulsations stop or sometimes until after delivery of placenta. Whereas, early or immediate cord clamping is typically performed within 15 seconds of delivery.[68]

## 3.3 CAUSES OF PRETERM BIRTH:

Preterm birth is a syndrome with a variety of causes. These can be broadly classified into two groups:

- Spontaneous preterm birth and
- Iatrogenic preterm birth.

  In iatrogenic/ induced preterm birth, the risk of continuing the pregnancy, to either the mother or the baby, is perceived as greater than the risks associated with preterm birth.[36]

Two thirds of preterm birth follow spontaneous onset of labour. Preterm birth can be due to:

- "Maternal" causes, related to a pre-existing maternal medical disorder, such as diabetes,
- "Obstetrical" or "Pregnancy related" causes, including hypertensive disorders, haemorrhage, and finally,
- "Fetal" causes.

Spontaneous preterm birth is regarded as a syndrome resulting from multiple causes. These include infection, inflammation and vascular diseases causing the uterus to change from quiescence to active contractions. The precise cause of spontaneous preterm labour remains unidentified in up to half of all cases.

Many maternal factors have been associated with an increased risk of spontaneous preterm birth. These include young or advanced maternal age, under 20 and over 40 years, short inter-pregnancy intervals, black race, periodontal disease, low maternal body mass index, multiple pregnancy, pre-existing non-communicable disease, hypertensive disorders of pregnancy, infections.[5,37-39] Fetus with congenital

malformations are also at a higher risk of preterm birth. A family history of preterm deliveries is a very strong risk factor.[40] But the strongest risk factor is a prior preterm birth. Woman with a history of spontaneous preterm birth has a 2.5-fold increased risk of preterm delivery in her next pregnancy.[41] Epidemiologic studies suggest that there is a genetic susceptibility to preterm birth. The heritability of preterm birth is estimated to be around 25–40%.[42] It was suggested that the influences of genetic background on a common, complex condition such as preterm birth occur in the context of an environmental milieu, and it is presumably this convergence that produces the phenotype of preterm birth.[43]

The events leading to preterm birth are still not completely understood. The etiology of preterm is thought to be multi factorial. It is, however, unclear whether preterm birth results from the interaction of several pathways or the independent effect of each pathway. Causal factors linked to preterm birth include medical conditions of the mother or fetus, genetic influences, environmental exposure, infertility treatments, behavioral and socioeconomic factors and iatrogenic prematurity.[5]

Thus, approximately 45–50% of preterm births are idiopathic, 30% are related to preterm premature rupture of membranes (PPROM) and another 15–20% is attributed to medically indicated or elective preterm deliveries.[34, 35] Estimation of preterm birth rates and, ideally, their proper categorization (e.g. spontaneous versus indicated) are essential for accurate determination of global incidence. This helps in forming policies and programmes on interventions to reduce the risk of premature labour and delivery.[43]

## 3.4 INCIDENCE

Preterm birth rates have been reported to range from 5% to 7% of live births in some developed countries, but are estimated to be substantially higher in developing countries.[33] These figures appear to be on the rise.[5]

## 3.5 COMPLICATIONS ASSOCIATED WITH PRETERM NEONATES

Preterm birth is a pervasive disorder that impacts all the functioning of a child with a high risk of pathological conditions on short and long term basis.

These include short term problems in the first weeks of life like - Respiratory distress syndrome (RDS), transient tachypnea of the newborn (TTN), apnoea, patent ductus arteriosus (PDA), hypotension, pulmonary hypertension, intraventricular hemorrhage, hypothermia, poor feeding, necrotizing Enterocolitis (NEC), anemia, jaundice, hypoglycaemia and sepsis.

On a long term basis, these sequelae have the potential to impact the neurodevelopment, education, behaviour, psychosocial, growth and health outcome. Many of these children, during preschool years, show regulatory problems, Attention Deficit Hyperactivity Disorder (ADHD) and Autism Spectrum Disorders (ASD). Periventricular Leukomalacia is a common and serious problem in the preterm population.[44] The most common long term neurodevelopmental disability associated with preterm birth is cerebral palsy. Epilepsy associated to cerebral palsy or not, is also more common with a prevalence of about 31%.[40] Approximately one third of all preterm infants have some cognitive impairment, 7% are severely impaired and a further 14% have mild cognitive impairment.[45]

Besides preterm infants are more likely to be readmitted to hospital, due to problems related to prematurity or to respiratory illness. Up to 40% of preterm

survivors suffer from bronchopulmonary dysplasia in spite of prenatal steroids and surfactant treatment. Its incidence is differently distributed in gestational age: it varies from 67% of the extremely preterm, to 37% among the very preterm.[46,47] Necrotizing enterocolitis is almost exclusively seen in preterm infants with an incidence between 4% and 7%, roughly one third of children needing surgery, a mortality rate between 12% and 30% and surviving infants at higher risk of long term problems as shown by the ORACLE Children Study.[48] Up to 3% of very preterm infants suffer from retinopathy of prematurity with severe visual impairment in up to 8% of tiniest infants. Other frequent problems are myopia and hypermetropia. Hearing impairment is stable at around <3–5% in low gestational age, nevertheless, these children are about 25 times more likely to be hearing impaired than the general population.[40]

## 3.6 MEASURES TO OPTIMISE THE NEONATAL OUTCOME IN PRETERM NEONATES

Neonatal outcome depends on the neonatal age, place and facilities for care at birth. As the preterm birth rate has not declined, advances in perinatal care have to be dramatically increased to ensure their survival even in extreme gestational ages.

Interventions to improve the outcome of preterm neonates can be at three levels: primary (directed to all women), secondary (aimed at eliminating or reducing risks), or tertiary (planned to improve outcomes for babies). Most of the successful efforts have been tertiary interventions. This includes regionalized care, use of surfactants, antibiotics, NICU care, advances in neonatal resuscitation techniques and ventilatory and fluid management, progress in surgery and anaesthesia.

Even some obstetric interventions like screening for asymptomatic bacteriuria, antenatal corticosteroid, prophylactic progesterone, prophylaxis for group B streptococcus has contributed to the decline in neonatal mortality.

Because of the heavy burden of morbidity, disability and mortality for premature babies and their families and excess costs for society, the main goal is to prevent premature births through an optimal prenatal care. This can be accomplished through organized systems of perinatal care in which mothers at risk are looked after in institutions with obstetric and neonatal specialists. Specialized neonatal transport, when needed, is also an important tool. Furthermore, paediatricians can aid the transition to adult health care by being aware of the nutritional, cardiovascular, respiratory, motor, cognitive, psychiatric and functional outcomes of preterm babies.[44]

## 3.7 NEONATAL ANEMIA IN PRETERM NEONATES

Newborn anemia associated with preterm birth is a common problem. There are three main causes of anemia: physiological mechanisms inherent to preterm birth, neonatal diseases or disorders, and more importantly, the frequent blood extractions for laboratory tests during intensive care.

In spite of specific strategies to limit transfusions, the great majority of preterm infants born at less than 32 completed weeks gestation receive at least one blood transfusion. The problems associated with anemia in preterm infants, as well as with its treatment (blood transfusions), are multiple and involve significant risks. Anemia hinders normal growth and contributes to postnatal malnutrition in most very-low-birth-weight preterm infants. They need hospitalization for a long time. Also, anemia interferes with the process of recovery from respiratory diseases (particularly bronchopulmonary dysplasia), congenital heart diseases, and bacterial infections. On

the other hand, blood or blood product transfusions may represent a significant risk for the transmission of infections and other diseases, especially in under-resourced settings.[9]

## 3.8 DELAYED CORD CLAMPING IN PRETERM NEONATES: TIME FOR CHANGE OF PRACTICE?

In virtually all mammal births, the umbilical cord remains a blood conduit from placenta to new-born for minutes to hours after birth.[15]

Physiologic studies in term infants have shown that a transfer from the placenta of approximately 80 mL of blood occurs by one minute after birth, reaching approximately 100 mL at three minutes after birth. This additional blood can supply extra iron, amounting to 40–50 mg/kg of body weight. This extra iron, combined with body iron (approximately 75 mg/kg of body weight) present at birth in a full-term newborn, may help prevent iron deficiency during the first year of life.[61]

Several systematic reviews have suggested that clamping the umbilical cord in all births should be delayed for at least 30–60 seconds, with the infant maintained at or below the level of the placenta because of the associated neonatal benefits, including increased blood volume, reduced need for blood transfusion, decreased incidence of intracranial haemorrhage in preterm infants, and decreased frequency of iron deficiency anaemia in term infants.

In addition, a longer duration of placental transfusion after birth may be beneficial because this blood is enriched with immunoglobulins and stem cells, which provide the potential for improved organ repair and rebuilding after injury from disorders caused by preterm birth. Although the magnitude of the benefits from

enhanced placental stem cell transfusion has not been well studied, the other neonatal benefits have led investigators to consider revising umbilical cord clamping practice guidelines.[61]

Delayed cord clamping has received increasing attention in the management at birth of preterm neonates. It seems to be beneficial and safe, associated with lesser delivery room resuscitation interventions, improved hemodynamic stability and decreased rates of intraventricular hemorrhage.[68]

DCC may increase the neonates blood volume by as much as 8% to 24% because continued blood flow through the fetal – placental unit facilitates placental transfusion to neonate. This is like a physiological process, letting a natural process occur at birth instead of iatrogenically interrupting it.[67]

This topic is being studied more and more lately in the premature infant. Delayed cord clamping in the term infant has been a practice. However there is still certain anxiety about its application in preterm neonates.

Recently studies have suggested delayed cord clamping to be associated with better neonatal outcomes in premature neonates. Recent studies involving very preterm and very low birth weight infants documented a higher hematocrit and red cell volume,[19,25,70] lower incidence of intraventricular hemorrhage and late onset sepsis.[24] In two systematic reviews, Rabe et al concluded that delayed cord clamping in very low birth weight infants may be beneficial and appears to be safe.[17,69]

With reference to the higher hematocrit level at 6 weeks of age, Ultee et al recently showed that DCC is associated with a higher hematocrit levels in late preterm infants at 10 weeks of age when compared with those with ECC.[26]

A retrospective meta-analysis was conducted by Rabe et al.[17] They reviewed infants born below 37 weeks gestation and enrolled into a randomized study of delayed cord clamping (30 seconds or more) versus immediate cord clamping (less than 20 seconds) after birth. They analyzed the results of 10 studies. A total of 454 preterm infants were described which met the inclusion and assessment criteria. Major benefits of the intervention were higher circulating blood volume during the first 24 h of life, less need for blood transfusions (p=0.004) and less incidence of intraventricular hemorrhage (p=0.002). There was no statistically significant differences were found between the groups for cord blood pH (mean difference, 0.01; 95% CI, –0.03–0.05), APGAR scores (RR for 5-minute APGAR score of less than 8, 1.17; 95% CI, 0.62–2.2), and body temperature at admission (mean difference, 0.14 °C; 95% CI, –0.31–0.03). Benefits of delayed umbilical cord clamping included a reduced need for blood transfusions for low blood pressure (RR, 0.39; 95% CI, 0.18 to 0.85) and anaemia (RR, 0.49; 95% CI, 0.31–0.81). No significant differences were noted for infant deaths (RR, 0.71; 95% CI, 0.3–1.69), but a significant reduction in the incidence of intraventricular haemorrhage with delayed umbilical cord clamping was reported by 7 of the10 published studies (RR, 0.53; 95% CI, 0.35–0.79).

Recent studies have shown a lower incidence of late onset sepsis and Intraventricular hemorrhage with delayed cord clamping.[24] The lower incidence of sepsis is based on the rationale that effective placental transfusion provided additional amount of stem cells that may confer additional immunologic competence.[62,63] The lower incidence of intraventricular hemorrhage is due to additional blood volume that provides circulatory stability for the latter.

More recently, Hosono and coworkers introduced a novel method of umbilical cord milking instead of delayed cord clamping to achieve placental transfusion for very preterm infants. They demonstrated that such procedure resulted in a higher blood pressure and urine outputs during the first 12 hours of life[64], shorter duration of assisted ventilation and less need for blood transfusion.[65] The merit of delayed cord clamping has been magnified as it is known that umbilical cord blood contains various valuable stem cells such as hematopoietic stem cells, endothelial cell precursors, mesenchymal progenitors and multipotent/pluripotent lineage stem cells.[55] It appears that in very preterm infants, placental transfusion achieved by delayed cord clamping or umbilical cord milking is a relatively inexpensive and safe intervention that could provide significant benefits.

A RCT was conducted by Williams Oh et al in 2011. Thirty three infants were randomized: 17 to the immediate cord clamping (ICC, cord clamped at 7.9 ± 5.2 seconds, m ± SD) and 16 to the delayed cord clamping (DCC, cord clamped at 35.2 ± 10.1 seconds) group. The study showed that, the hematocrit was higher in the DCC group (45 ± 8 versus 40 ± 5%, $p<0.05$). The frequency of events during delivery room resuscitation was almost identical between the two groups. There was no difference in hourly mean arterial blood pressure during the first 12 hours of life. A difference in the incidence of selected neonatal morbidities and hematocrit at 2, 4 and 6 weeks as well as the need for transfusion was noted, but none of the differences was statistically significant. Thus the study concluded that a higher hematocrit is achieved by delayed cord clamping in very low birth weight infants suggesting effective placental transfusion.[21]

In a RCT by McDonnell M et al to assess: (i) the size of placental transfusion following a 30 seconds delay in cord clamping following vaginal and cesarean births and (ii) the feasibility of delaying cord clamping in the labour ward and particularly in the operating theatre. It was noted that there were trends towards higher mean hematocrit in the infants following delayed clamping, but these were not significant either at 1 hour (55 ± 7.7 vs. 52.9 ± 7) or at 4 hour of age (55 ± 7 vs. 52.5 ± 7). The trends were more marked in the infants born by cesarean section, and in those born at 26-29 weeks gestation.[66]

Thus this study concluded that a 30 seconds delay in cord clamping is feasible at both vaginal and cesarean births, but does not lead to the predicted difference in infant hematocrit. Although physiological studies suggest that a placental transfusion of 15-20 mL/kg occurs within 30 seconds of delivery, these data suggest that future trials should either delay cord clamping for more than 30 seconds, or should alter the position of the infant in relation to the uterus in order to facilitate the transfusion. The study also proposed that delayed cord clamping is feasible at cesarean section.[66]

A study by Kaempf W J et al on 77 VLBW neonates and 172 LBW neonates showed that delayed cord clamping can be safely performed in singleton premature neonates and is associated with higher hematocrit, less delivery room resuscitation and without any increase in untoward effects such as lower APGAR scores, polycythaemia, jaundice and respiratory distress.[15]

A RCT by Strauss et al showed that, circulating RBC volume / mass increased ($p = 0.04$) and weekly hematocrit (Hct) values were higher ($p = 0.70$). Apgar scores after birth and daily SNAP scores were not significantly different ($p = 0.22$). Requirements for mechanical ventilation with oxygen were similar. More neonates

needed phototherapy (p = 0.03) after delayed clamping, but initial bilirubin levels and extent of phototherapy did not differ.[20]

Thus the study concluded that although a one minute delay in cord clamping significantly increased RBC volume/mass and Hct, clinical benefits were modest. Clinically significant adverse effects were not detected. Thus proposing a one minute delay incord clamping to increase RBC volume/mass and RBC iron, for neonates 30 to 36 weeks gestation, who do not need immediate resuscitation.[20]

Cochrane Pregnancy and Childbirth Group did a meta-analysis of fifteen Studies (738 infants). Participants were between 24 and 36 weeks gestation at birth. The maximum delay in cord clamping was 180 seconds. Delaying cord clamping was associated with fewer infants requiring transfusions for anemia, less intraventricular hemorrhage and lower risk for necrotizing enterocolitis compared with immediate clamping.[4] Infants were born between 24 weeks of gestation and 36 weeks of gestation. The maximum delay in umbilical cord clamping was 180 seconds. Delaying umbilical cord clamping was associated with fewer infants who required transfusion for anaemia (seven trials, 392 infants; RR, 0.61; 95% CI, 0.46–0.81) and for low blood pressure (four trials with estimable data for 90 infants; RR, 0.52; 95% CI, 0.28–0.94) and less intraventricular haemorrhage (ultrasound diagnosis all grades) (10 trials, 539 infants; RR; 0.59; 95% CI, 0.41–0.85) compared with immediate umbilical cord clamping. For other outcomes (infant death, severe [grade 3–4] intraventricular haemorrhage, and periventricular leukomalacia), no clear differences were identified between groups; however, many trials were affected by incomplete reporting and wide confidence intervals. Outcome after discharge from the hospital was reported for one small study, and no significant differences were reported between the groups in

mean Bayley II scores at age 7 months (corrected for gestation at birth and involved 58 children).[18]

A Study by Dr. Isaac Blickstein Kaplan et al in Rehoboth Israel showed that, in preterm infants, delayed clamping appears to reduce the risk of intraventricular hemorrhage and the need for neonatal transfusion.[72]

Ross Sommers et al in 2012 conducted at prospective study in which twenty-five infants were enrolled in the DCC group and 26 in the ICC group. Gestational age, birth weight, and male gender were similar. Admission laboratory and clinical events were also similar. DCC resulted in significantly higher superior vena cava blood flow over the study period, as well as greater right ventricle output and right ventricular stroke volumes at 48 hours. No differences were noted in middle cerebral artery BFV, mean superior mesenteric artery BFV, shortening fraction, or the incidence of a persistent ductus arteriosus, concluded that DCC in premature infants is associated with potentially beneficial hemodynamic changes over the first days of life.[71]

ACOG committee opinion on timing on clamping umbilical cord in 2012, reaffirmed in 2014, showed evidences supporting delayed cord clamping in preterm neonates. As with term infants, delayed umbilical cord clamping to 30 – 60 secs after birth with the infant at a level below placenta is associated with establishment of red blood cell volume and decreased need for blood transfusion. The single most important clinical benefit for preterm is the possibility for a nearly 50% reduction in IVH. It is important to note that the timing of umbilical cord clamping should not be altered for the purpose of collecting umbilical cord blood for banking.[61]

Despite these evidences, early cord clamping has been practiced widely to facilitate management of third stage and allow immediate pulmonary resuscitation of the premature neonate. Immediate cord clamping is still the standard practice among obstetricians, as many obstetricians are concerned that delaying the clamping of the cord may compromise the welfare of an infant during delivery.

Thus although till date, a number of RCTs have been carried out to evaluate the benefits and adverse effects of delayed umbilical cord clamping in preterm neonates, few studies show conflicting results. Furthermore there is no clear cut consensus regarding the timing of delayed clamping of the umbilical cord. There are only a few studies evaluating the role of delayed umbilical cord clamping at cesarean sections. Many RCTs have evaluated the benefits of delayed umbilical cord clamping; the ideal time has yet to be established. Also the ideal time of umbilical cord clamping after cesarean section has to be determined, as preterm neonates who may be benefitted are likely to be born by cesarean section, because most of their mothers have medical and obstetric complications.

We conducted this clinical trial to gather additional evidence for efficacy of delayed cord clamping in preterm neonates in terms of improving the neonatal outcome as well as find an answer to the above questions.

# METHODOLOGY

The present study was conducted in the Department of Obstetrics and Gynecology, KLE University's Dr. Prabhakar Kore Hospital and Medical Research Centre, KLE University's teaching hospital attached to Jawaharlal Nehru Medical College, Belagavi.

**Study design**

The study design was a randomized controlled trial.

**Study period**

This study was conducted during the period from May 2014 to May 2015.

**Source of data**

Pregnant women with gestational age between 34 weeks to 36 weeks 6 days delivered either vaginally or by cesarean section in the labour room were included in the study.

**Sample size**

A total of 128 pregnant women delivering late preterm neonates were included in the study for analysis.

**Sampling technique**

The sample size was calculated considering two sample proportions, for the rate of 1minute APGAR score (of 5 in early cord clamping and as of 7 in delayed cord clamping ) of premature neonates using the formula as below,

$$n=\frac{2(Z\alpha+Z\beta)^2pq}{(p_0-p_1)^2}$$

Where,

n = number of samples

Zα= 1.96

Zβ= 0.84

$P_0$ = rate of 1 min APGAR of 7 among delayed cord clamping = 55%

$P_1$ = rate of 1 min APGAR of 5 among early cord clamping = 15%

$P = P_0 + P_1 /2$

q =100-p

With type I error rate α = 0.05 and

Type II error rate β = 0.02 with a power of 80%

Considering the above formula the minimum sample size was calculated as 128.

**Selection criteria**

**Inclusion Criteria**:

- Pregnant women delivering late preterm neonates between 34 weeks to 36 weeks 6 days period of gestation assigned by LMP and / or first trimester ultrasound and / or mid trimester anomaly scan

**Exclusion Criteria**:

- Neonates who need immediate resuscitation - neonates with bradycardia/ no respiratory effort/ meconium stained fluid/ concerning fetal heart rate pattern particularly those with suspected severe depression (like very low or undetectable heart rate)
- Pregnant women known to have fetal congenital malformations
- HbsAg and HIV positive mothers

- Rh negative pregnancy
- Multiple gestation
- Placental abnormalities such as placenta previa or accreta, vasa previa, suspected placental abruption

**Ethical clearance**

Prior to the commencement of the study ethical clearance was obtained from the Institutional Ethical committee, Jawaharlal Nehru Medical College, Belagavi. (Annexure I)

**Informed Consent**

All pregnant women between 34 weeks to 36 weeks 6 days period of gestation admitted to the labour room and delivering preterm live babies were screened for eligibility by detailed history, routine antenatal examination and investigations by trained residents in the department of obstetrics and gynecology. Those fulfilling the selection criteria were explained about the purpose of the study and the need for randomization. A written informed consent was obtained from all the participants before the enrollment (Annexure II).

**Method of collection of data**

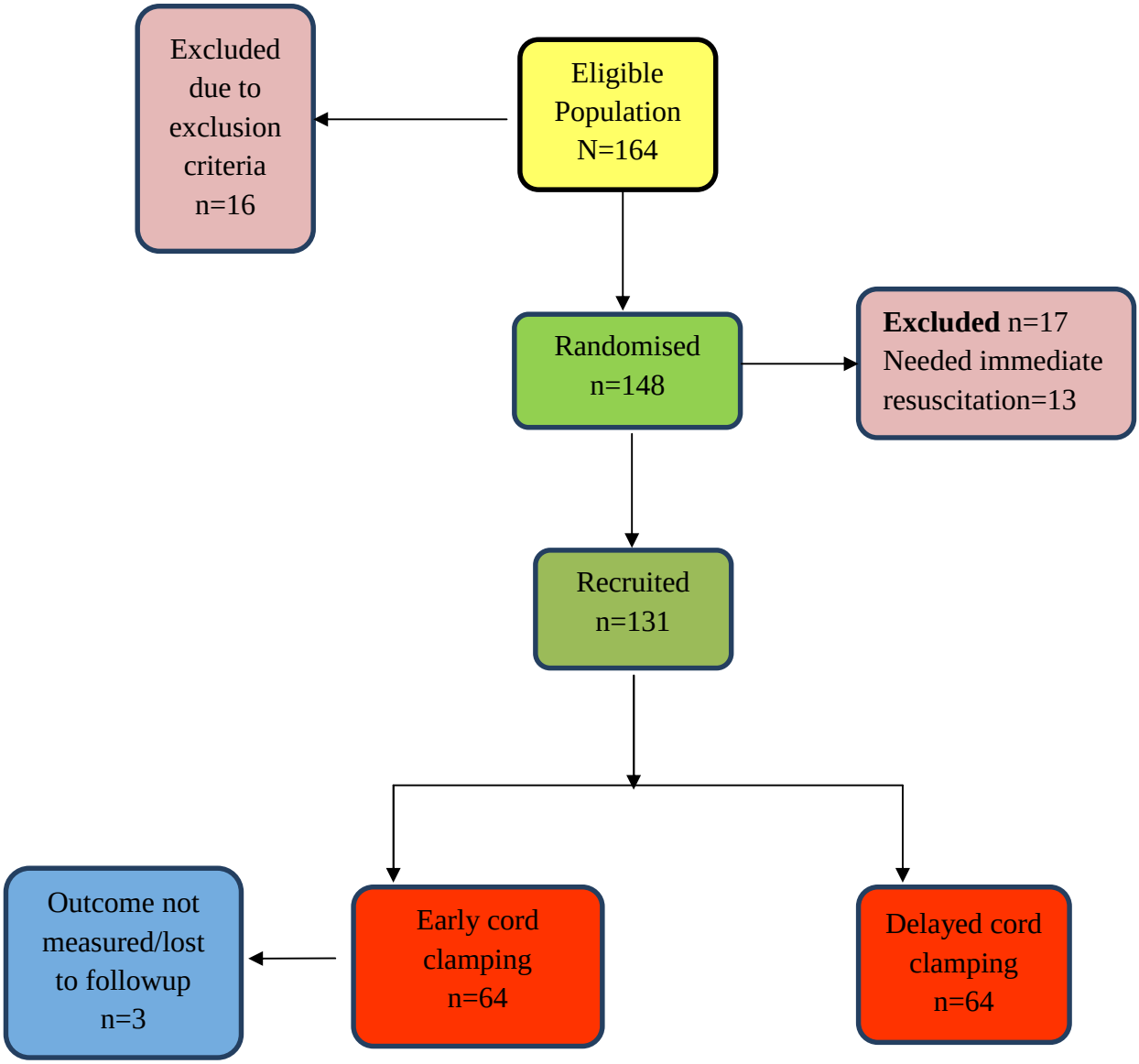
After enrollment demographic data, obstetric history, current pregnancy details, information on labour, mode of delivery was obtained. Routine obstetric examination was carried out. Neonatal outcome after delivery was obtained. The data was recorded on a predesigned and pretested proforma (Annexure III)

**Randomization**

Based on the computer generated randomization chart these pregnant women were randomized into groups as below.

- Study group (n = 64): included late preterm neonates subjected to delayed cord clamping.
- Control group (n = 64): included late preterm neonates subjected to early cord clamping.

**CONSORT Flow diagram**



**Procedure:**

The eligible pregnant women delivering late preterm neonates were randomly allotted to the study group or the control group using a computer generated randomization chart. The pregnant women randomized to the study group were subjected to delayed cord clamping. The pregnant women randomized to the control group were subjected to early cord clamping as per the routine hospital protocol. All pregnant women received at least one dose of steroids (Inj. Betamethasone 12 mg or Inj Dexamethasone 6 mg) upon admission to the labour room. The delivery was conducted by the trained residents of the department of obstetrics and gynaecology. In those women undergoing vaginal delivery, babies were placed on a sterile tray covered with a sterile warm towel at or just below the level of the introitus by the attending nurse. In those women undergoing cesarean delivery, babies were placed on sterile drapes between the mother's legs. All babies after birth were dried gently, stimulated and suctioning done if needed by the trained resident conducting the delivery. A stop clock was used to note the time of cord cutting from the delivery of the baby. The timer was started after delivery of the buttocks. Umbilical cord was cut after 45 seconds in the delayed cord clamping group and in the early cord clamping group, umbilical cord was clamped within 5 seconds of birth. The neonate was then handed over to the awaiting NICU team.

The neonatal outcome of all the cases was recorded in terms of:

- APGAR score at 1 and 5 minutes
- Hemoglobin in gm% on Day one of life (between 12 – 24 hours of life)

- Highest total and direct serum bilirubin level attained before discharge in mg/dl
- Adverse neonatal outcomes like NICU admissions and need for phototherapy for neonates with hyperbilirubinemia
- Neonatal mortality rate
- Gestational age at delivery
- Birth weight

**Photograph 1. Consent taking**

**Photograph 2. Cord clamping in preterm neonates during cesarean section**

**Photograph 3. Cord clamping in preterm neonates during vaginal delivery**

**Photograph 4. Routine neonatal resuscitation**

**Statistical analysis**

The data obtained was coded and entered into Microsoft Excel worksheet. The categorical data was expressed as rates, ratios and proportions and continuous data was expressed as mean ± standard deviation (SD). Data were statistically described as mean ± standard deviation or percentage (%) as appropriate. The comparison of quantitative variables was done with the use of student t test for independent samples. For comparing categorical data, chi-square test was performed. The data was analysed using chi-square test and Fischer's exact test. A probability value ('p' value) of less than or equal to 0.05 was considered as statistically significant. All statistical calculations were done with the use of the computer programs Microsoft Excel 2017 and SPSS version 17 for Microsoft windows.

# RESULTS

This one year randomized controlled trial was conducted in the Department of Obstetrics and Gynecology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, KLE University's teaching hospital attached to Jawaharlal Nehru Medical College, Belagavi, during the period from May 2014 to May 2015.

A total of 128 pregnant women who delivered late preterm neonates between 34 to 36 weeks 6 days gestation were analysed in the study. Based on the computer generated randomization chart these women were randomized into groups as below.

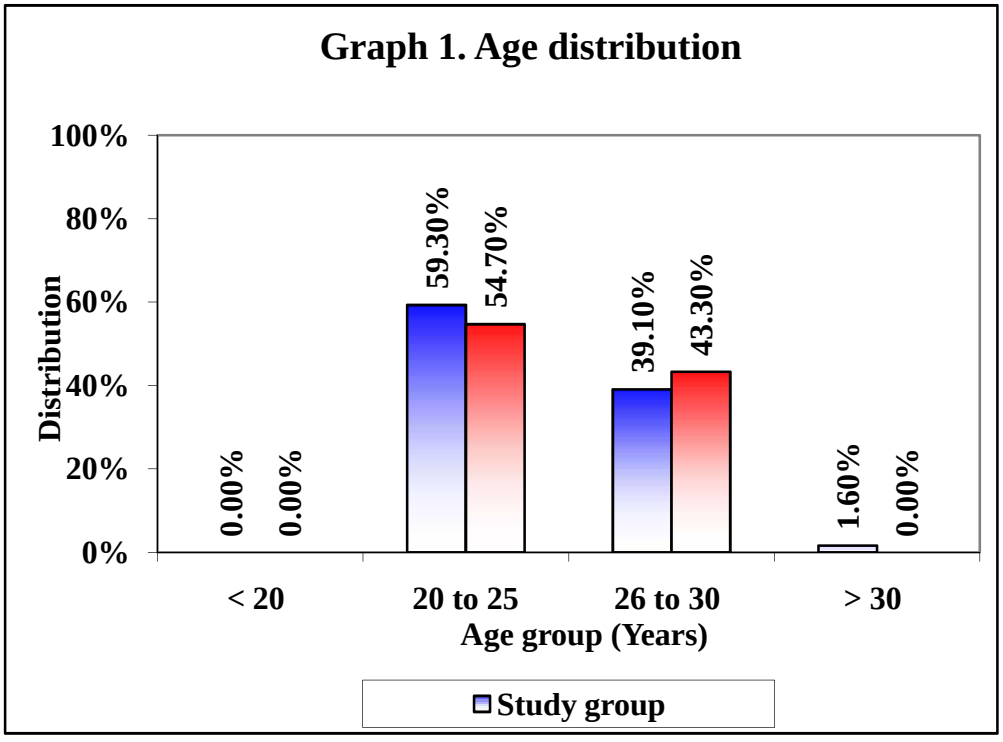
- Study group (n = 64): included pregnant women delivering late preterm neonates and subjected to delayed cord clamping.
- Control group (n = 64): included pregnant women delivering late preterm neonates and subjected to early cord clamping.

The data obtained was coded and entered into Microsoft Excel worksheet and the data was analyzed and results were tabulated as below.

**Table 1 . Maternal Age distribution**

| Age group (Years) | DCC group (n=64) | | ECC Group (n=64) | |
|---|---|---|---|---|
| | Number | Percent | Number | Percent |
| < 20 | 0 | 0 | 0 | 0 |
| 20 to 25 | 38 | 59.3 | 35 | 54.7 |
| 26 to 30 | 25 | 39.1 | 29 | 45.3 |
| > 30 | 1 | 1.6 | 0 | 0 |
| **Total** | **64** | **100.00** | **64** | **100.00** |

**Chi square value = 0.291 DF= 1 p= 0.592**




In the present study, majority of pregnant women that 59.3% in the DCC group and 54.7 % women in ECC group were aged between 20 to 25 years. Whereas 39.1% in the DCC and 43.3% in the ECC group were between 26 – 30 years. p value = 0.592 was not statistically significant.

**Table 2. Mean maternal age**

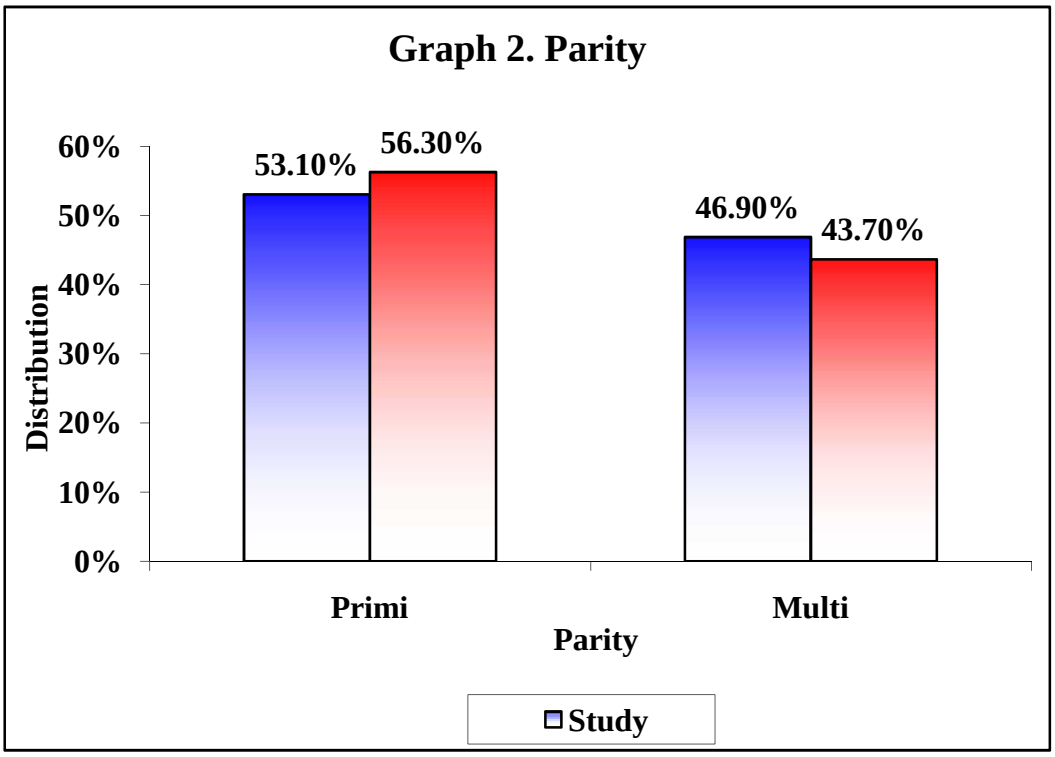
| Age (Years) | DCC group (n=64) | ECC group (n=64) |
|---|---|---|
| Mean | 24.8 | 25.01 |
| SD | 2.64 | 2.62 |
| Median | 25 | 25 |
| Maximum | 31 | 30 |
| Minimum | 20 | 20 |
| t value = 0.451 | DF= 126 | p= 0.625 |

The mean maternal age in DCC group was 24.8 ± 2.64 years and the median age was 25 years with range being 20 to 31 years. In ECC group the mean age was 25.01± 2.62 years and the median age was 25 years with range between 20 to 30 years. p value= 0.625. Hence there was no statistically significant difference in the maternal age distribution in the DCC and the ECC group.

**Table 3. Parity**

| Parity | DCC group (n=64) | | ECC Group (n=64) | |
|---|---|---|---|---|
| | Number | Percent | Number | Percent |
| Primi | 34 | 53.1 | 36 | 56.3 |
| Multi | 30 | 46.9 | 28 | 43.7 |
| **Total** | **64** | **100.00** | **64** | **100.00** |

**Chi square value = 0.133 DF= 1 p = 0.722**

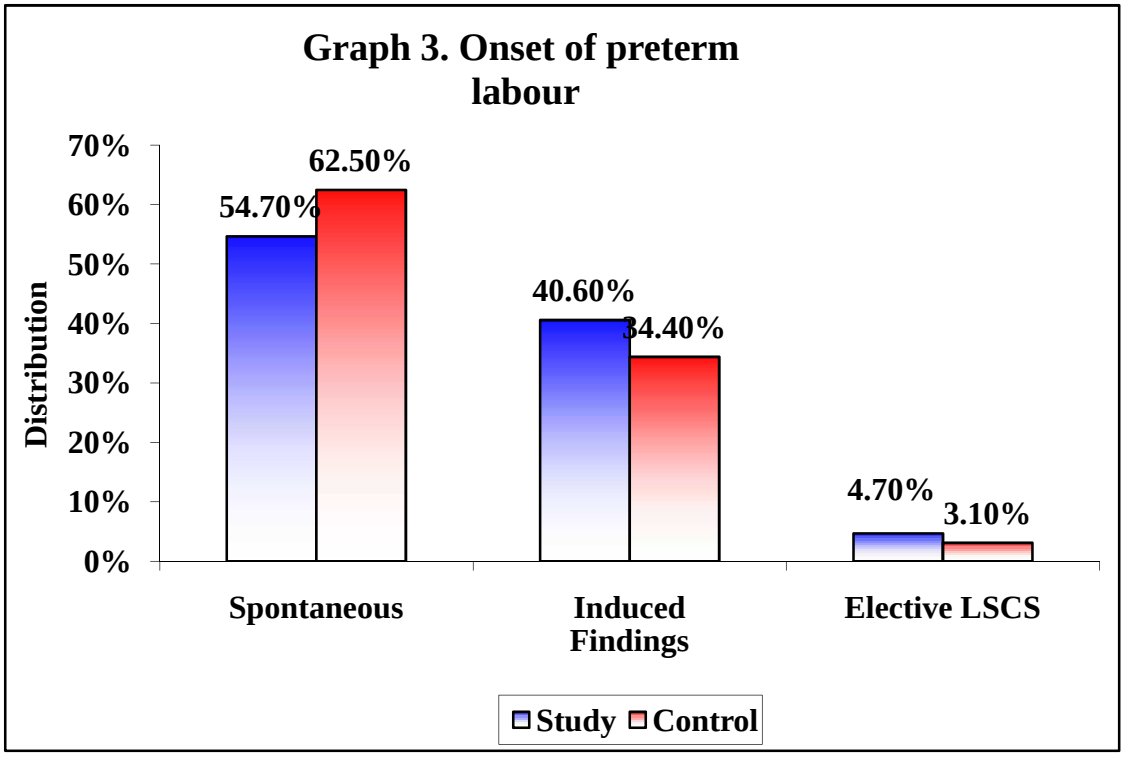



In the present study, 53.1 % of the pregnant women in the DCC group and 56.3 % of the pregnant women in the ECC group were primigravida. (p = 0.722) was not statistically significant.

**Table 4: Mode of Onset of preterm labour**

| Findings | DCC group (n=64) | | ECC group (n=64) | |
|---|---|---|---|---|
| | Number | Percent | Number | Percent |
| Spontaneous | 35 | 54.7 | 40 | 62.5 |
| Induced | 26 | 40.6 | 22 | 34.4 |
| Elective LSCS | 03 | 4.7 | 02 | 3.1 |
| **Total** | **64** | **100.00** | **64** | **100.00** |

**$x^2$ = 0.8667 DF = 2 p = 0.648**

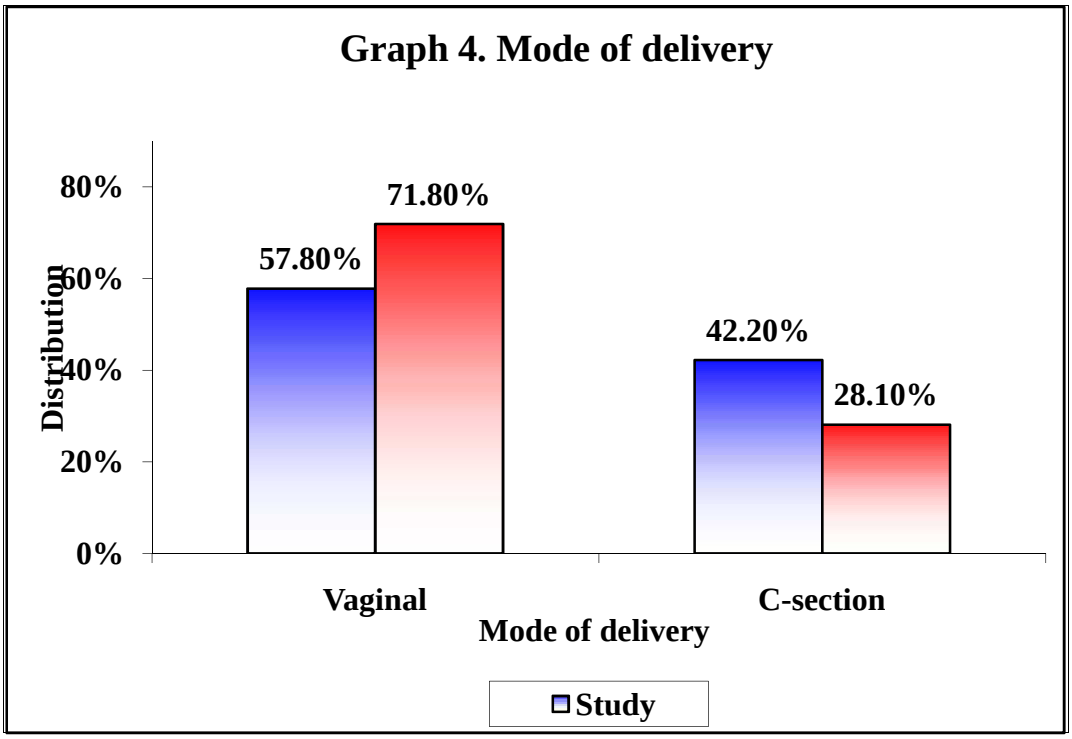



In the present study, majority of pregnant women that is 54.70% in the DCC group and 62.50% of the pregnant women in the ECC group had spontaneous onset of labour. p value = 0.648. This difference was not statistically significant.

**Table 5: Mode of delivery**

| Mode of delivery | DCC group (n=64) | | ECC Group (n=64) | |
|---|---|---|---|---|
| | Number | Percent | Number | Percent |
| Vaginal | 37 | 57.8 | 46 | 71.8 |
| C-section | 27 | 42.2 | 18 | 28.1 |
| **Total** | **64** | **100.00** | **64** | **100.00** |

**$x^2$ = 2.775 DF = 1 p = 0.09**

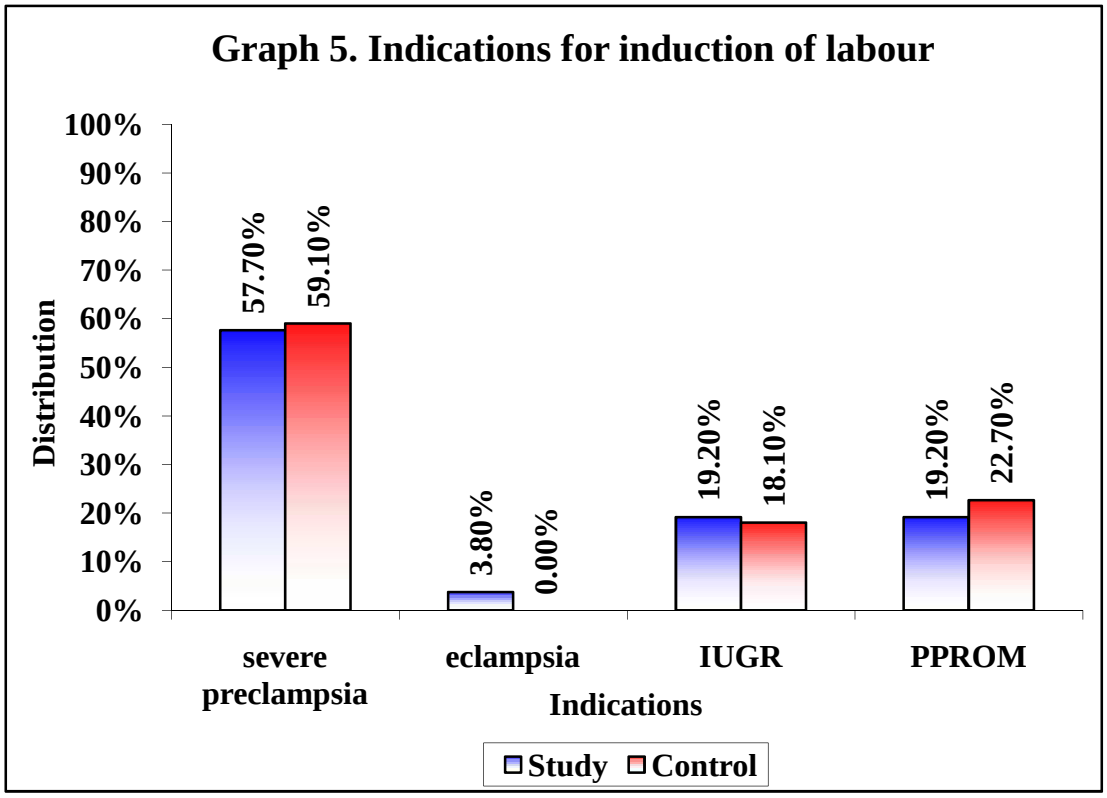



In the present study, majority of the pregnant women that is 57.8% in the DCC group and 71.8% of the pregnant women in the ECC group had vaginal delivery. 42.2% of the pregnant women in the DCC group and 28.1% of the pregnant women in the ECC group had cesarean section. (p value = 0.09). There was no statistically significant difference in the mode of delivery in the two groups.

**Table 6: Indications for induction of labour**

| Indications | DCC group (n=26) | | ECC Group (n=22) | |
|---|---|---|---|---|
| | Number | Percent | Number | Percent |
| Severe Preeclampsia | 15 | 57.7 | 13 | 59.1 |
| Eclampsia | 1 | 3.8 | 0 | 0 |
| IUGR | 5 | 19.2 | 4 | 18.1 |
| PPROM | 5 | 19.2 | 5 | 22.7 |

$x^2$ = 0.927 p = 0.818

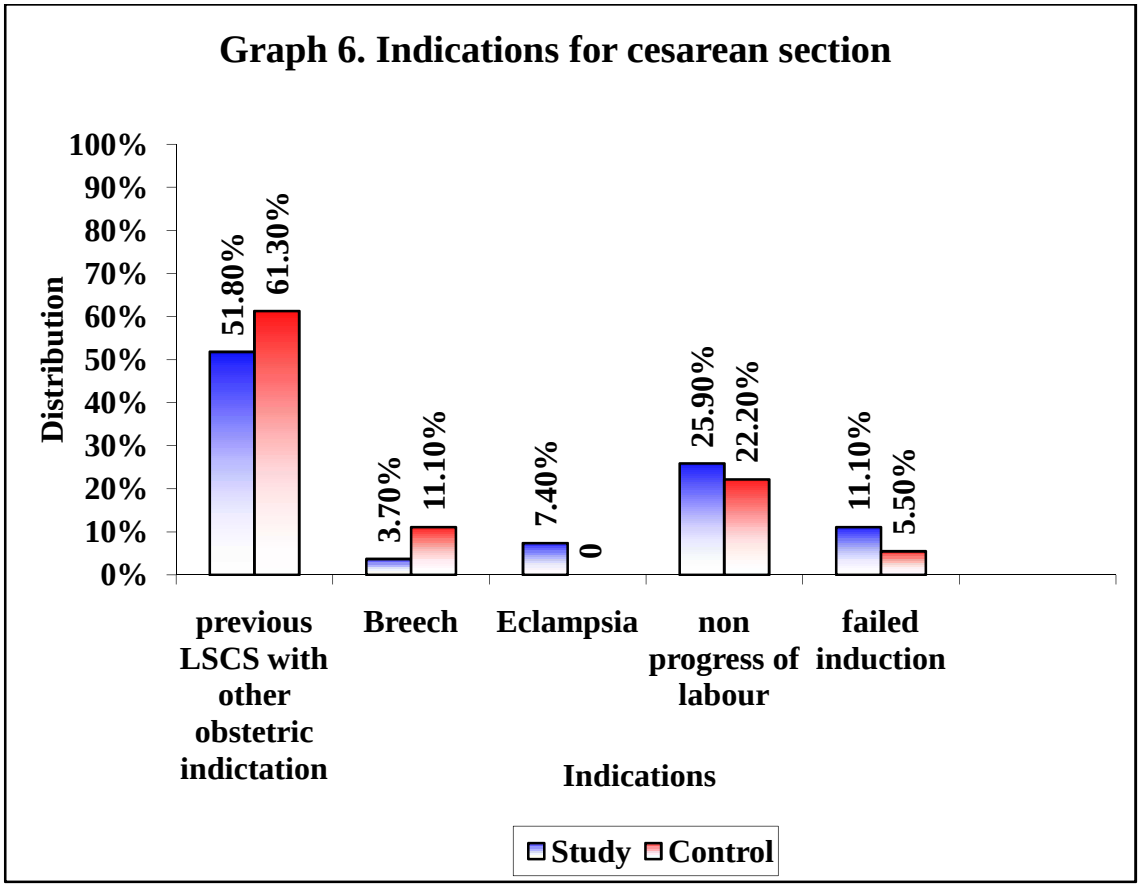



In the present study, severe preeclampsia was the major cause for induction of labour, seen in 57.7% of the pregnant women in the DCC group and 59.10% in the ECC group. p value = 0.818. Hence there was no statistically significant difference in the indications for induction of labour in the two groups.

**Table 7: Indications for cesarean section**

| Indications | DCC group (n=27) | | ECC Group (n=18) | |
|---|---|---|---|---|
| | Number | Percent | Number | Percent |
| Previous LSCS with other obstetric indications | 14 | 51.8 | 11 | 61.3 |
| Breech | 1 | 3.7 | 2 | 11.1 |
| Eclampsia | 2 | 7.4 | 0 | 0 |
| Non progress of labour | 7 | 25.9 | 4 | 22.2 |
| Failed induction | 3 | 11.1 | 1 | 5.5 |

**$x^2$ = 2.824 p=0.587**

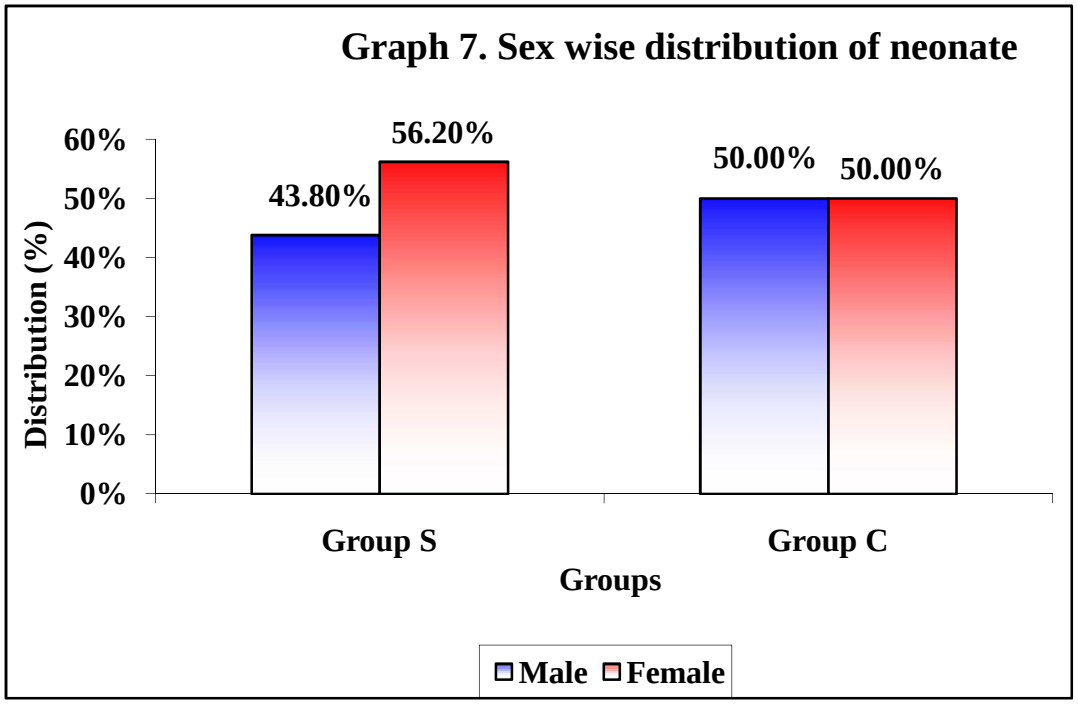



In the present study, most common indication for cesarean delivery was previous LSCS with other obstetric indications ( like Previous LSCS with PPROM, CPD, Polyhydramnios, not willing for TOLAC, previous 2 LSCS) that is 51.80% in the DCC group and 61.30% in the ECC group. p value = 0.587. Indications for cesarean delivery were not significantly different in the two groups.

**Table 8: Sex wise distribution of neonate**

| Sex | DCC (n=64) | | ECCs (n=64) | |
|---|---|---|---|---|
| | **Number** | **Percentage** | **Number** | **Percentage** |
| Male | 28 | 43.8% | 32 | 50.0% |
| Female | 36 | 56.2% | 32 | 50.0% |
| **Total** | **64** | **100.00** | **64** | **100.00** |

**Chi-square** **p = 0.595**

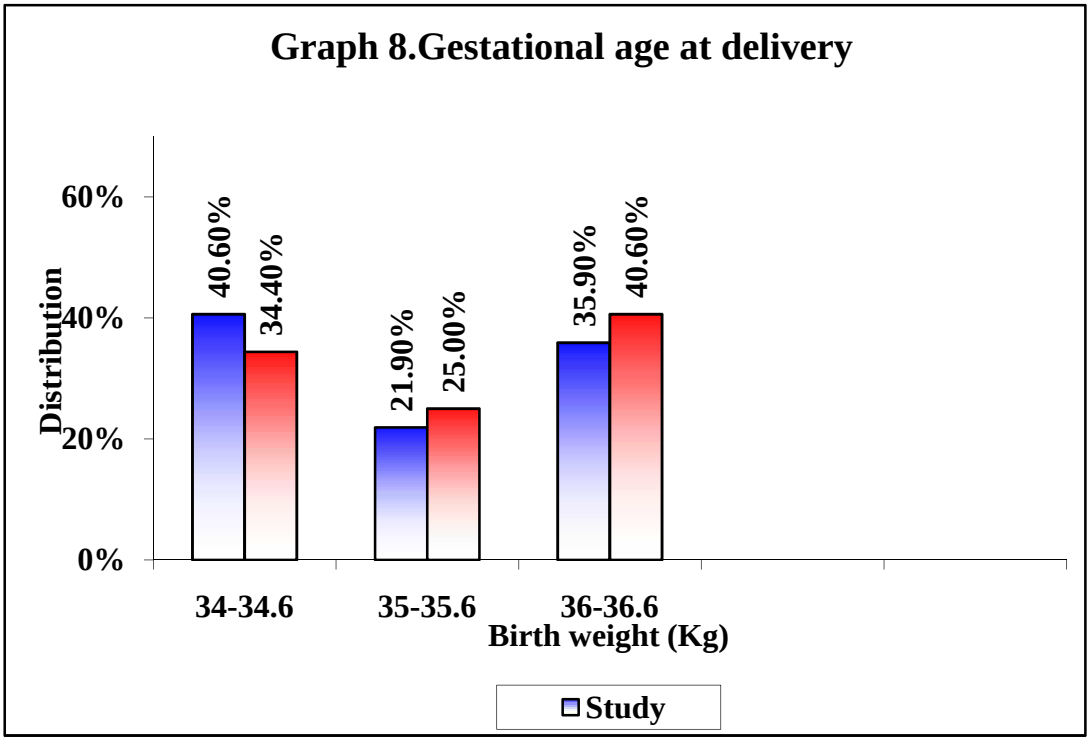



In this study, among DCC group, 56.2% were females compared to 50.0% in ECC (p = 0.595). No statistically significance difference in age distribution.

**Table 9. Gestational age at delivery**

| Gestational age | DCC group (n=64) | | ECC Group (n=64) | |
|---|---|---|---|---|
| (Weeks) | Number | Percent | Number | Percent |
| 34.0- 34.6 | 27 | 42.2 | 22 | 34.4 |
| 35- 35.6 | 14 | 21.9 | 16 | 25.0 |
| 36-36.6 | 23 | 35.9 | 26 | 40.6 |
| **Total** | **64** | **100.00** | **64** | **100.00** |

**$x^2$ value = 0.641 DF= 2 p = 0.725**




In the present study, majority of the pregnant women that is 42.2% in the DCC group and 34.4% in the ECC group had gestational age between 34 weeks - 36.6 weeks period of gestation. Whereas 21.9% in the DCC group and 25% in the ECC group had gestational age between 35 – 35.6 weeks period of gestation. p value = 0.725. There was no significant difference in the distribution of gestational age at delivery between the DCC and ECC group.

**Table 10. Mean gestational age**

| Gestational age (weeks) | DCC | ECC |
|---|---|---|
| Mean | 35.23 | 35.3 |
| SD | 0.87 | 0.92 |
| Median | 35.1 | 35.3 |
| Maximum | 36.6 | 36.6 |
| Minimum | 34 | 34 |

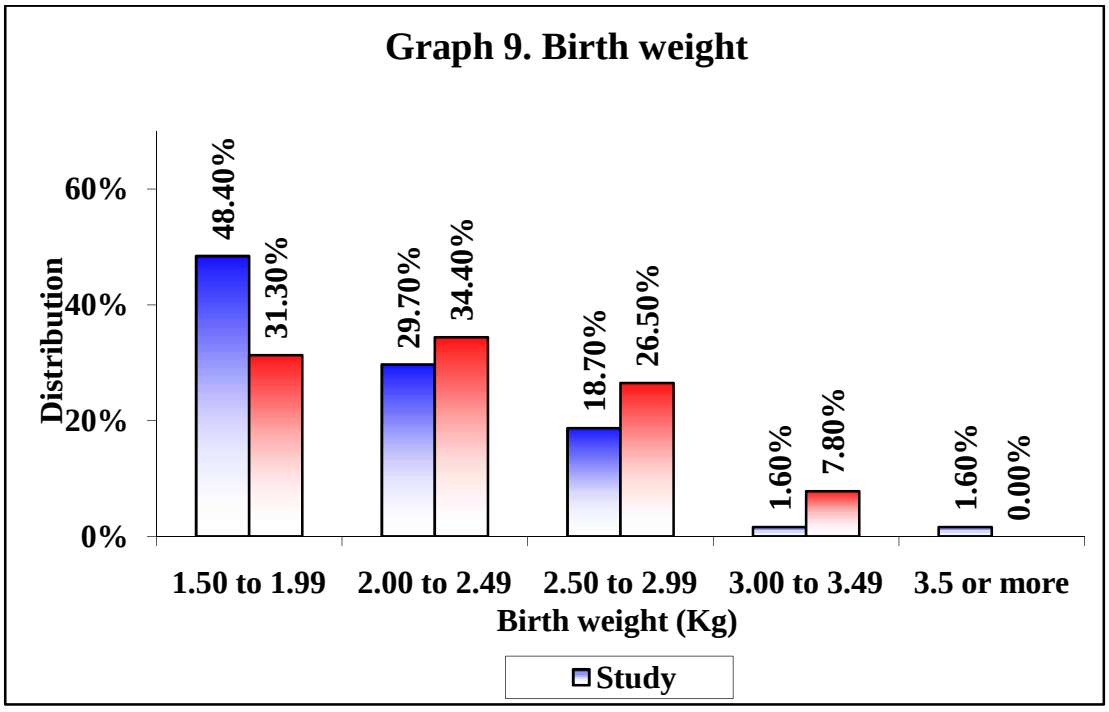
**t value = 0.4423** **DF= 126** **p= 0.659**

The mean gestational age at delivery in the DCC group was 35.23 ± 0.87weeks and the median was 35.1 weeks with range between 34 to 36.6 weeks. In the ECC group, mean gestational age at delivery was 35.3 ± 0.92 weeks and the median was 35.3 weeks with range being the same as in DCC group.

**Table 11. Birth weight wise distribution of neonate**

| Birth weight (Kg) | DCC group (n=64) | | ECC Group (n=64) | |
|---|---|---|---|---|
| | Number | Percent | Number | Percent |
| 1.50 to 1.99 | 31 | 48.4 | 20 | 31.3 |
| 2.00 to 2.49 | 19 | 29.7 | 22 | 34.4 |
| 2.50 to 2.99 | 12 | 18.7 | 17 | 26.5 |
| 3.00 to 3.49 | 1 | 1.6 | 5 | 7.8 |
| 3.5 or more | 1 | 1.6 | 0 | 00 |
| **Total** | **64** | **100.00** | **64** | **100.00** |

$x^2$ = **4.744** **DF = 5** **p = 0.192**




In the present study, 48.40% in the DCC group and 31.30% in the ECC group had birth weight between 1.5kgs and 1.99 Kgs, while 29.70% in the DCC group and 34.0% in the ECC group had birth weight between 2 Kgs to 2.49 Kgs. p value = 0.192. There was no significant difference in the distribution of birth weights of the neonate in DCC and ECC groups.

**Table 12. Mean birth weight of the neonate**

| Birth weight (Kg) | DCC | ECC |
|---|---|---|
| Mean | 2.18 | 2.31 |
| SD | 0.50 | 0.48 |
| Median | 2.1 | 2.3 |
| Maximum | 3.7 | 3.2 |
| Minimum | 1.5 | 1.5 |

**t value = 1.5005** **DF= 126** **p= 0.1360**

The mean birth weight in the DCC group was 2.18 ± 0.50 Kgs and the median birth weight was 2.1 Kgs with range between 1.5 to 3.7 Kgs. In the ECC group, mean birth weight was 2.31± 0.48 Kgs and the median was 2.3 Kgs with range between 1.5 to 3.2 Kgs. However this difference was not statistically significant (p value = 0.136).

**Table 13. APGAR score at 1 min**

| APGAR score | DCC group (n=64) | | ECC Group (n=64) | |
|---|---|---|---|---|
| | **Number** | **Percent** | **Number** | **Percent** |
| At 1 Min | | | | |
| < 7 | 38 | 59.37 | 35 | 54.68 |
| > 7 | 26 | 40.63 | 29 | 45.31 |
| **Total** | **64** | **100.00** | **64** | **100.00** |
| Chi square value = 0.293 | | DF =1 | p value = 0.592 | |

**Table 14. APGAR scoreat 5 Min**

| | | | | |
|---|---|---|---|---|
| < 7 | 4 | 6.25 | 3 | 4.69 |
| > 7 | 60 | 93.75 | 61 | 95.31 |
| **Total** | **64** | **100.00** | **64** | **100.00** |

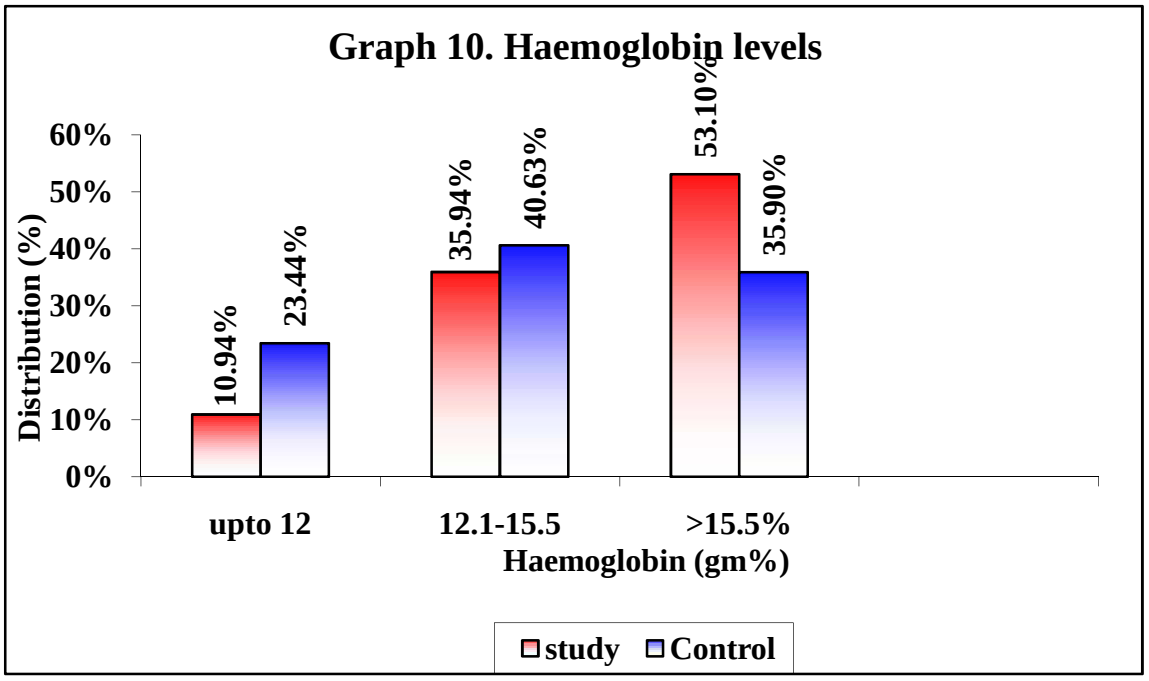
**Chi square value with Yate's correction = 0 p = 1**

In the present study, APGAR score at 1 min < 7 was among 59.37% and 54.68% in the ECC group respectively. p value = 0.592. This difference was not statistically significant.

**Table 15. Distribution of haemoglobin levels in gram% on day one of life**

| Haemoglobin (gm %) | DCC (n=64) | | ECC (n=64) | |
|---|---|---|---|---|
| | Number | Percentage | Number | Percentage |
| Up to 12 | 7 | 10.94 | 15 | 23.44 |
| 12.1 to 15.5 | 23 | 35.94 | 26 | 40.63 |
| Above 15.5 | 34 | 53.1 | 23 | 35.9 |
| **Total** | **64** | **100.00** | **64** | **100.00** |

**Chi-square = 5.215** **DF= 2** **p = 0.0736**




In this study, hemoglobin levels between 12.1 – 15.5 gm percent was noted in 35.94% and 40.63% in the DCC and ECC group respectively. And hemoglobin levels above 15.5 gm% were noted in 53.1% and 35.9% in the DCC and ECC group respectively. p value = 0.0736. Hence there was no significant difference in the distribution of hemoglobin levels in the two groups.

**Table 16. Mean haemoglobin levels in gram% on day one of life**

| Hemoglobin (gram %) | DCC | ECC |
|---|---|---|
| Mean | 15.66 | 14.05 |
| SD | 3.12 | 3.07 |
| Median | 15.5 | 14.3 |
| Maximum | 21.4 | 21.4 |
| Minimum | 4.1 | 5.3 |

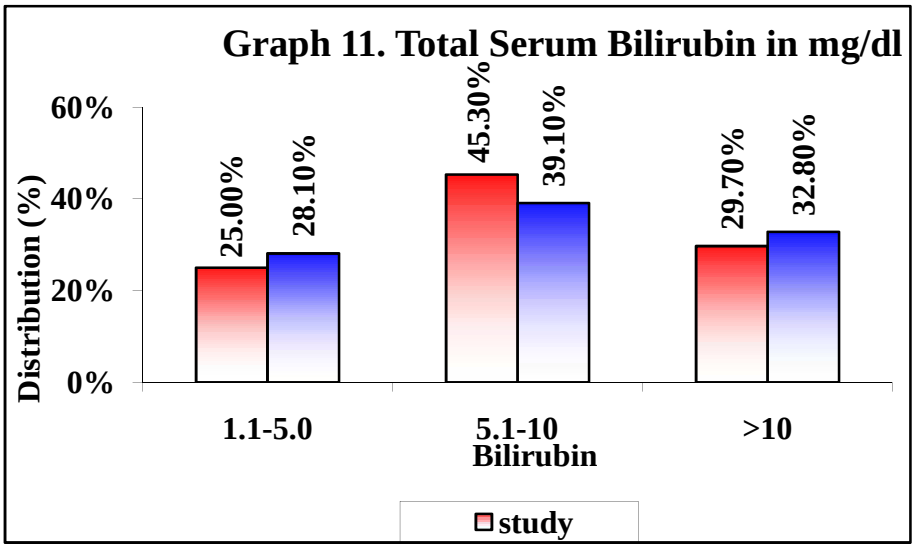
**t value =2.9426 DF= 126 p= 0.0039**

Mean Haemoglobin levels in gram% on day one of life of neonates among DCC was 15.66 with SD of 3.12 and among ECCs were 14.05 with SD of 3.07. p value = 0.0039, which is very statistically significant. Thus hemoglobin levels in the DCC group were significantly higher in the DCC group compared to the ECC group.

**Table 17. Peak Total serum bilirubin levels in mg/dl attained before discharge**

| Bilirubin | DCC (n=64) | | ECC (n=64) | |
|---|---|---|---|---|
| | **Number** | **Percentage** | **Number** | **Percentage** |
| 1.1 to 5.0 | 16 | 25 | 18 | 28.1 |
| 5.1 to 10 | 29 | 45.3 | 25 | 39.1 |
| Above 10 | 19 | 29.7 | 21 | 32.8 |
| **Total** | **64** | **100.00** | **64** | **100.00** |

**Chi square value = 0.513 DF = 2 p = 0.773**



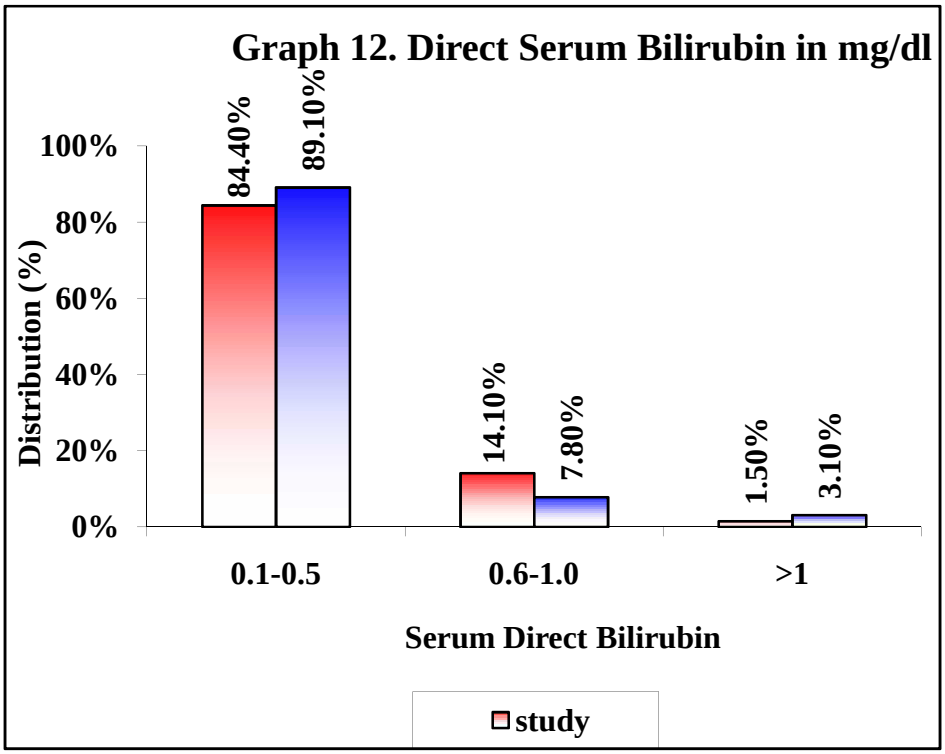

Total serum bilirubin levels between 5.1 mg/dl to 10 mg/dl were among 45.3% and 39.1% in the DCC and ECC group respectively. And total serum bilirubin levels between 1.1 mg/dl to 5.0 mg/dl were among 25% in the DCC group and 28.1% in the ECC group. P value = 0.773. This difference was not statistically significant.

Mean total serum Bilirubin (mg/dL) among was 7.92 with SD of 3.61 and among ECCs were 8.03 with SD of 3.18. p value= 0.8552, which is not statistically significant.

**Table 18. Peak direct serum bilirubin levels in mg/dl attained before discharge**

| Bilirubin | DCC (n=64) | | ECC (n=64) | |
|---|---|---|---|---|
| | Number | Percentage | Number | Percentage |
| 0.1 to 0.5 | 54 | 84.4 | 57 | 89.1 |
| 0.6 to 1.0 | 9 | 14.1 | 5 | 7.8 |
| Above 1 | 1 | 1.5 | 2 | 3.1 |
| **Total** | **64** | **100.00** | **64** | **100.00** |

**Chi square value= 1.566 DF= 2 p = 0.459**




In the study, 84.4% had direct serum bilirubin levels between 0.1 to 0.5 mg/dl and among ECCs, 89.1% had direct serum bilirubin between 0.1 to 0.5 mg/dl. While 14.10% and 7.80% had direct serum bilirubin levels between 0.6-1.0 mg/dl in the DCC and ECC group respectively. p value = 0.459. Hence the difference in serum

direct bilirubin levels in mg/dl between the DCC and ECC group was not statistically significant.

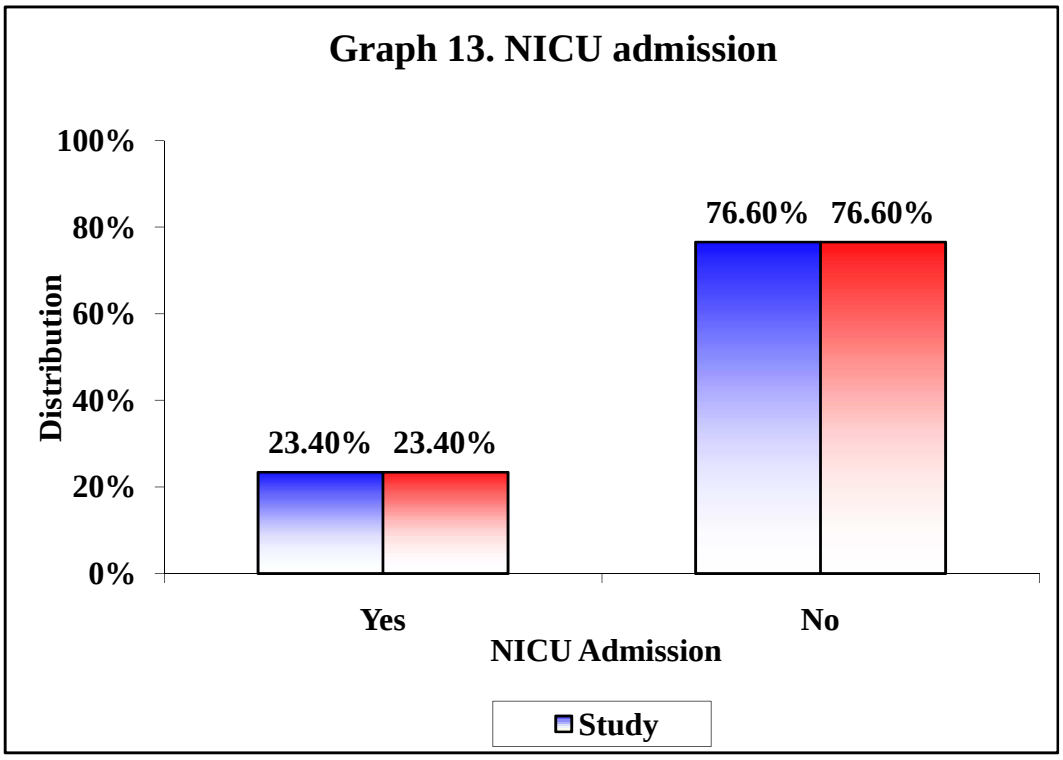
Mean direct serum Bilirubin (mg/dL) among DCC was 0.40 with SD of 0.198 and among ECCs was 0.371 with SD of 0.229. p value = 0.449, which is not statistically significant.

Hence there was no statistically significant difference in the serum bilirubin levels (total and direct) in the DCC and ECC group.

**Table 19. NICU admissions**

| NICU admission | DCC group (n=64) | | ECC Group (n=64) | |
|---|---|---|---|---|
| | **Number** | **Percent** | **Number** | **Percent** |
| Yes | 15 | 23.4 | 15 | 23.4 |
| No | 49 | 76.6 | 49 | 76.6 |
| **Total** | **64** | **100.00** | **64** | **100.00** |

**Chi square value = 0** **DF= 1** **p = 1**

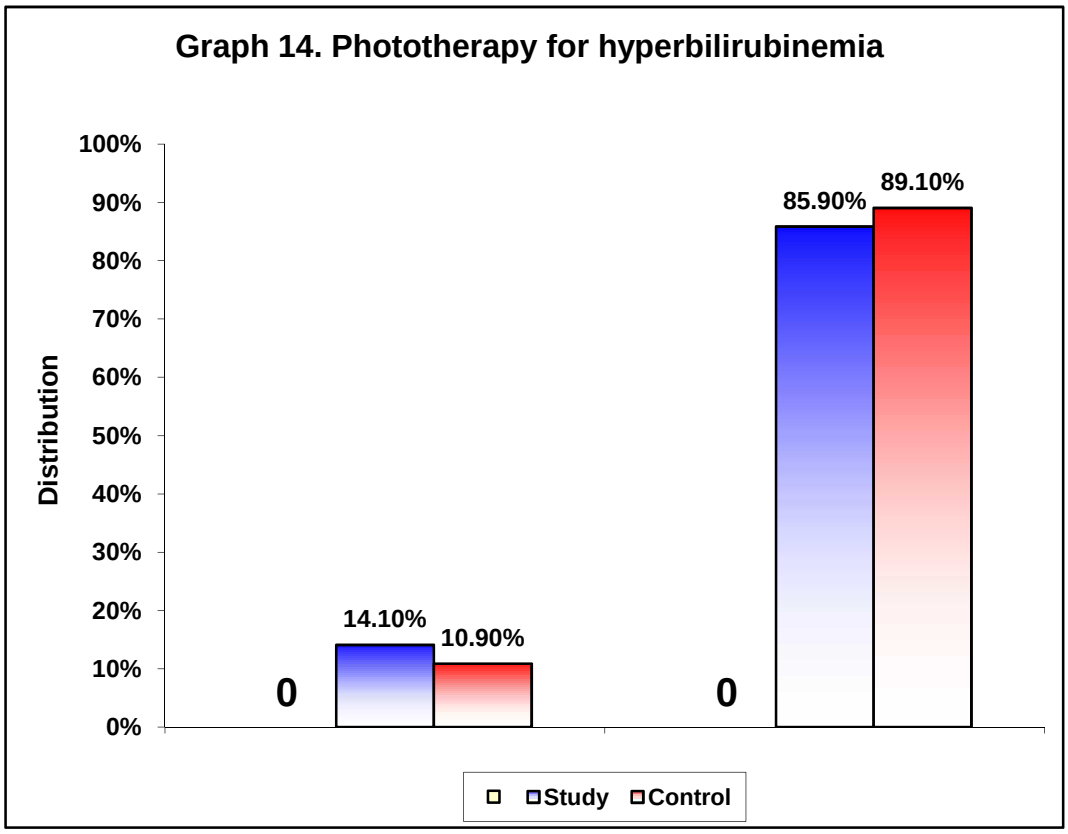



In the present study, the rate of NICU admissions in the DCC group and ECC group was the same, 23.4%. p value = 1.

**Table 20. Phototherapy for hyperbilirubinemia**

| Phototherapy | DCC group (n=64) | | ECC Group (n=64) | |
|---|---|---|---|---|
| | Number | Percent | Number | Percent |
| Yes | 09 | 14.1 | 07 | 10.9 |
| No | 55 | 85.9 | 57 | 89.1 |
| **Total** | **64** | **100.00** | **64** | **100.00** |

**Chi square value = 0.2857** **DF= 1** **p = 0.592**




In the present study, majority of the preterm neonates did not need phototherapy. In the DCC group, 14.10% needed phototherapy versus 10.90% in the ECC group. p value = 0.592 was not statistically significant.

**Table 21. Pregnancy outcome**

| Pregnancy outcome | DCC group (n=64) | | ECC Group (n=64) | |
|---|---|---|---|---|
| | **Number** | **Percent** | **Number** | **Percent** |
| Live birth | 63 | 98.4 | 63 | 98.4 |
| Fresh macerated stillbirth | 0 | 0 | 0 | 0 |
| Macerated still Birth | 0 | 0 | 0 | 0 |
| Early neonatal death | 1 | 1.6 | 1 | 1.6 |
| **Total** | **64** | **100.00** | **64** | **100.00** |

Chi square test with Yate's correction = 0 p = 1

There was no difference in the pregnancy outcome in the two groups.

# DISCUSSION

Timing of umbilical cord clamping after delivery has long been a matter of controversy. Immediately after the birth, the cord pulsates and placenta continues to provide oxygen, red blood cells, stem cells, immune cells and blood volume to the baby. This is called placental transfusion. Delayed cord clamping facilitates this process ensuring safe oxygen levels and blood volume for the baby. Several studies have concluded the beneficial effect of delaying the clamping of umbilical cord by 30 – 180 seconds in preterm neonates in terms of increase in hematocrit, fewer transfusions for anemia, less delivery room resuscitation and mechanical ventilation by providing for placental transfusion of additional volume of blood from placenta to the baby. The other benefits being decrease in incidence of intraventricular hemorrhage (IVH) and late onset sepsis.

In 2012, the American College of Obstetricians and Gynecologists (ACOG) published a committee opinion on the timing of umbilical cord clamping after birth, which was also endorsed by the American Academy of Pediatrics. The current recommendations support delaying cord clamping in preterm neonates for 30 – 60 secs after delivery with the neonate held at or below the level of the placenta. [61]

Despite the evidence and recommendations for DCC, there is reluctance by the neonatal/ obstetrical community to adopt this theory and a lot of anxiety and concern regarding welfare of preterm neonate associated with delayed cord clamping, that it may interfere with immediate resuscitation of the preterm neonates, as the premature neonates are at increased risk of temperature dysregulation, hypotension, and are at need for immediate pediatric assessment and blood transfusion. Most of the obstetricians and mid wives still practice early cord clamping in preterm neonates

which was an age old practice adopted presumably to facilitate management of third stage of labour and immediate resuscitation of premature neonates. For example, a survey of policy at 1175 units in 14 European countries found that two-thirds clamped the cord immediately after birth, although 90% routinely administered prophylactic uterotonics.[73]

Several studies conclude in favor of delayed cord clamping in preterm neonates with DCC also shown to decrease the overall incidence of IVH. But the enthusiasm for DCC is tempered by the lack of benefit for severe IVH and small number of infants included in these trails. The lack of benefit could reflect lack of adequate placental transfusion during DCC for infants delivered by cesarean delivery. Three trails of DCC that stratified by mode of delivery found no difference in hematocrit levels or tagged red blood cells in infants delivered by cesarean delivery. The ACOG acknowledges that there are limited data indicating whether DCC performed during cesarean delivery can improve placental transfusion. Thus there is no consensus on the optimal timing of clamping the umbilical cord and its feasibility during cesarean section.

As it is difficult to assess objectively the additional blood volume transferred to the neonate, indirect measures in the form of measurement of venous hematocrit, mean arterial blood pressure, urine output, serum bilirubin levels, need for assisted ventilation, oxygen therapy, need for blood transfusions, incidence of IVH have been used as measures to evaluate the effects of placental transfusion among the various studies.

The present study was undertaken to compare the effect of delayed versus early cord clamping in late preterm neonates on hemoglobin levels at day one of life

(12 – 24 hours) and peak serum bilirubin levels attained before discharge. The secondary objective was to assess the effect of delayed cord clamping on adverse neonatal outcomes.

This one year randomized controlled trial was conducted in the Department of Obstetrics and Gynecology, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi during the period of May 2014 to May 2015. A total of 128 pregnant women between 34 weeks to 36 weeks 6 days period of gestation admitted to the labour room and delivering preterm live babies were included in the study. Based on the computer generated randomization chart these pregnant women were randomized into two groups, study group which included pregnant women with late preterm neonates subjected to delayed cord clamping and control group which included pregnant women with late preterm neonates subjected to early cord clamping. Umbilical cord was cut after 45 seconds in the delayed cord clamping group and in the early cord clamping group, umbilical cord was clamped within 5 seconds of birth. In those women undergoing vaginal delivery, babies were placed at or just below the level of the introitus. And during cesarean section, babies were placed introitus between the mother's legs.

In the present study, the two groups were matched in terms of demographic parameters like maternal age and parity like in most other studies.[23, 70, 15]

Majority of pregnant women that is 59.3% of in the DCC group and 54.7 % women in ECC group were aged between 20 to 25 years of age, whereas 39.1% in the DCC and 43.3% in the ECC group were between 26 – 30 years of age. p value = 0.592. Hence there was no statistically significant difference in the maternal age distribution in the DCC and ECC group.

The mean age in DCC group was 24.8 ± 2.64 years and in ECC group the mean age was 25.01 ± 2.62 years. p value= 0.625 was not statistically significant.

53.1 % of the pregnant women in the DCC group and 56.3 % of the pregnant women in the ECC group were primigravida. p = 0.722. This difference was not statistically significant

In our study, mechanism of onset of labour, mode of delivery, indication for induction of labour and indication for LSCS were matched between the two groups.

Majority of pregnant women that is 54.70% in the DCC group and 62.50% of the pregnant women in the ECC group had spontaneous onset of labour. p value = 0.648. This difference was not statistically significant.

Majority of the pregnant women that is 57.8% in the DCC group and 71.8% of the pregnant women in the ECC group had vaginal delivery. 42.2% of the pregnant women in the DCC group and 28.1% of the pregnant women in the ECC group had cesarean section (pvalue = 0.09). There was no statistically significant difference in the mode of delivery in the two groups.

This finding was consistent with the study by Kugelman Et al[23] in which infants born by cesarean section compared with vaginal deliveries were significantly smaller (1569 ± 417 versus 1882 ± 528 grams; p = 0.06 in ICC group, and 1409 ± 402 versus 2029 ± 411 grams; p <0.0005 in DCC group, respectively). Infants born by cesarean section compared with vaginal deliveries were significantly smaller (1569 ± 417 versus 1882 ± 528 grams; p = 0.06 in ICC group, and 1409 ± 402 versus 2029 ± 411 grams; p <0.0005 in DCC group, respectively).

In this study, sex of the neonate, gestational age at delivery and birth weights were matched between the two groups.

Among DCC group, 56.2% of the neonates were females compared to 50.0% in ECC (p=0.595). No statistically significance difference in sex distribution was noted.

Majority of the pregnant women that is 42.2% in the DCC group and 34.4% in the ECC group had gestational age between 34 weeks 34.6 weeks period of gestation, whereas 21.9% in the DCC group and 25% in the ECC group had gestational age between 35 – 35.6 weeks period of gestation. p value = 0.725. There was no significant difference in the gestational age distribution at delivery between the DCC and ECC group.

The mean gestational age at delivery in the DCC group was 35.23 ± 0.87 weeks and in the ECC group, mean gestational age at delivery was 35.3 ± 0.92 weeks (p = 0.659).

In the present study, 48.40% in the DCC group and 31.30% in the ECC group had birth weight between 1.5 Kgs and 1.99 Kgs, while 29.70% in the DCC group and 34.0% in the ECC group had birth weight between 2 Kgs to 2.49 Kgs. p value = 0.192. There was no significant difference in the distribution of birth weights of the neonate in DCC and ECC groups.

The mean birth weight in the DCC group was 2.18 ± 0.50 Kgs. In the ECC group, mean birth weight was 2.31± 0.48 Kgs. This difference was not statistically significant (p value = 0.136).

Thus the present study included neonates between 34 – 36.6 weeks gestation (late preterm neonates) and with birth weights >1500 grams. However, in contrast most of the studies conducted previously to study the effect of umbilical cord clamping at birth in preterm neonates included neonates with gestational ages ranging between 24 – 32 weeks or neonates with LBW (<2000 grams) and VLBW ( < 1500 grams). A RCT conducted by Mercer et al in 2003[70] included 32 neonates with gestational ages between 24 – 32 weeks. A RCT by McDonnell et al in 2007[66] included 46 neonates with gestational ages between 26 – 33 weeks. A prospective RCT by Kugelman et al in 2007[23] included 65 neonates between 24 weeks to < 35 weeks. A RCT by William Oh et al in 2011[21] included 33 neonates between 24 – 28 weeks. In a prospective randomized partially blinded study by Strauss et al in 2008[20] included 158 neonates below 36 weeks which were analysed into two subgroups of large preterm neonates between 30 – 36 weeks and small preterm neonates < 30 weeks. A RCT by Utlee et al in 2008[26] studied 37 premature neonates between 34 – 36 weeks gestation. In the RCT conducted by J.Kaempf et al in 2012[15] included 249 neonates who were analysed into two subgroups of VLBW (401- 1500 grams ) and LBW neonates ( > 1500 grams but less than 35 weeks) .

With respect to the time of delaying umbilical cord clamping, by definition, early cord clamping is done immediately after delivery between 5 – 15 seconds and in delayed cord clamping, clamping the cord is delayed between 25 seconds up to 5 minutes after delivery. Majority of the studies conducted so far have considered a delay in cord clamping between 30 – 45 seconds,[70,29,21] with range between 30 seconds up to 3 minutes. In a study[66] which compared the effect with a delay of 30 secs suggested the need for longer delay to demonstrate significant increase in hematocrit. A study conducted by Strauss et al[15] studied the effect of delaying cord

clamping by 60 seconds which coincided with timing for 1 minute APGAR score. In the study by Utlee et al[26] in one group cord was clamped at 30 seconds and in the other group, cord was clamped at 3 minutes.

In the present study, we evaluated the effect of delaying cord clamping by 45 seconds versus immediate cord clamping within 5 seconds, which we considered to be a safe cut off to demonstrate the beneficial effect of delayed cord clamping in terms of increased hematocrit without adverse outcomes. And also because 45 seconds was felt to be the mid-point of the delay in cord clamping in majority of delayed cord clamping studies in premature neonates.

In terms of the outcomes measured, the findings of our study is consistent with several studies conducted on preterm neonates which have shown that delayed cord clamping leads to significantly increased circulating blood volume (beneficial effect) in terms of hematocrit, blood pressures, without significant adverse effect in terms of increase in serum bilirubin levels, need for phototherapy, exchange transfusions, decreased APGAR score, NICU admissions rates and neonatal mortality.

Several indirect measures have been used to measure the increase in blood volume among the various studies.

In the present study, we considered measuring mean hemoglobin levels as an indirect measure of blood volume. Mean hemoglobin levels in gram % on day one of life of neonates among DCC were 15.66 with SD of 3.12 and among ECC were 14.05 with SD of 3.07. p value= 0.0039, which is statistically significant. Thus the mean hemoglobin level in the DCC group was significantly higher in the DCC group compared to the ECC group.

A pilot study conducted by Mercer J. S. et al in 2003, to assess the feasibility of delayed cord clamping in VLBW neonates measured mean arterial blood pressure over first four hours. Adjusting for gestational age, infants in DCC (32 ± 12 versus 6.2 ± 3 secs) groups were three times more likely to have mean BP above 30 mm Hg, as additional placental transfusion augments immediate blood volume of the infant.[70]

In 2007, Mc Donnell et al conducted a feasibility study in which venous hematocrit was measured at 1 and 4 hour of age. The study demonstrated higher mean hematocrit following DCC but these were not significant at either 1 hour (55 ± 7.7 vs. 52.9 ± 7) or 4 hour of life (55 ± 7 vs. 52.5 ± 7). The trends were higher in infants born by caesarean section and those born at 26 – 29 weeks. The study recommended future trails with delayed clamping > 30 seconds and altering the position of infant relative to the uterus to facilitate transfusion. This study also concluded that DCC is feasible during cesarean delivery.[66]

A study conducted by Kugelman et al in 2007, found a tendency for higher initial diastolic blood pressure (36 ± 11 versus 32 ± 7 mm Hg; p = 0.07), higher initial Hct, and higher mean 24-hour Hct in DCC compared with the ICC group. These effects were more pronounced in the vaginally delivered neonates: initial Hct, mean 24-hour Hct, red blood cells (5.2 ± 0.34 versus 4.4 ± 0.6 million/mm3; p = 0.01), and Hct >55% (six versus one neonate; p= 0.02), all were significantly higher in the DCC group. Initial mean blood pressure on admission to the NICU in neonates <1500 grams tended to be higher in the DCC group, in the total cohort, and in cesarean deliveries. There was no differences in initial systolic blood pressures; in any measurements of blood pressure at 4,12, and 24 hours; in the means of the first 24

hours; or in the need for vasopressors in the first 12 hours of life (one and two neonates in the ICC or DCC group, respectively).[23]

A RCT by Utlee et al in 2008 studied neonatal and follow up data for the effects of early versus delayed cord clamping. The late cord-clamped group showed consistently higher hemoglobin levels than the early cord-clamped group, both at the age of 1 hour (mean (SD) 13.4 (1.9) mmol/l vs. 11.1 (1.7) mmol/l), and at 10 weeks (6.7 (0.75) mmol/l vs. 6.0 (0.65) mmol/l).[26]

A RCT conducted by Strauss et al in 2008, compared the hematologic and clinical effects of delayed cord clamping by 1 min versus early cord clamping in preterm neonates < 36 weeks. The primary end points were increase in RBC volume/ mass, per biotin labeling. Secondary endpoints were multiple clinical and laboratory comparisons over first 28 days including score for neonatal acute physiology (SNAP). This study also had similar findings in comparison to our study. Circulating RBC volume/ mass and weekly hematocrit values were higher $p = 0.04$ and $p < 0.005$ respectively. But it did not lead to fewer RBC transfusions ($p \geq 0.72$).[20]

In 2008, Rabe et al conducted a systematic review and metanalysis of a brief delay in clamping the umbilical cord of preterm infants, in which results of 10 studies describing 454 preterm infants were analysed. They also had similar conclusions in favour DCC with higher circulating blood volume during first 24 hours of life, less need for blood transfusions ($p = 0.004$), also less incidence of intraventicular hemorrhage.[17]

A RCT conducted by William Oh et al in 2011 on VLBW infants also had similar conclusion. DCC was done at 35.2 ± 10.1 seconds and ICC was done at 7.9 ± 5.2 seconds. The study showed hematocrit to be higher in DCC group (45 ± 8 versus

40 ± 5 %). At 2, 4, 6 weeks of age, and at the time of discharge, hematocrit was still higher in DCC group but not statistically significant. There were no differences in neonatal morbidities. There was no difference in hourly mean arterial blood pressures during first 12 hours of life.[21]

In 2000, Rabe in a study pointed out that, delayed cord clamping for 45 seconds is feasible and safe in preterm neonates below 33 weeks and also that it is possible during cesarean delivery. It reduces the need for packed cell transfusions during the first 6 weeks of life.[25]

In a study conducted by Joseph Kaempf et al in 2012, VLBW and LBW neonates who underwent delayed cord clamping, had significantly higher hematocrit. p value = 0.02 and < 0.01 respectively. But delayed cord clamping did not significantly lower the overall red blood cell transfusion rate. Delayed cord clamping was associated with higher mean systolic and diastolic blood pressures in LBW (p = 0.03).[15]

In terms of adverse neonatal outcome, in the present study, mean total serum bilirubin (mg/dL) among DCC was 7.92 with SD of 3.61 and among ECC were 8.03 with SD of 3.18. p value= 0.8552, which is not statistically significant. Total serum bilirubin levels between 5.1 mg/dl to 10 mg/dl were among 45.3% and 39.1% in the DCC and ECC group respectively. And total serum bilirubin levels between 1.1 mg/dl to 5.0 mg/dl were among 25% in the DCC group and 28.1% in the ECC group. p value = 0.773. This difference was not statistically significant.

In the study, mean direct serum bilirubin (mg/dL) among DCC was 0.40 with SD of 0.198 and among ECC was 0.371 with SD of 0.229. p value = 0.449, which is not statistically significant. 84.4% had direct serum bilirubin levels between 0.1 to

0.5 mg/dl and among ECC, 89.1% had direct serum bilirubin between 0.1 to 0.5 mg/dl. While 14.10% and 7.80% had direct serum bilirubin levels between 0.6-1.0 mg/dl in the DCC and ECC group respectively. p value = 0.459. Hence the difference in serum direct bilirubin levels in mg/dl between the DCC and ECC group was not statistically significant.

Hence there was no statistically significant difference in the serum bilirubin levels (total and direct) in the DCC and ECC group.

In the present study, there was no increase in the need for phototherapy for hyperbilirubinemia in the delayed cord clamping group as compared to early cord clamping group. In the DCC group, 14.10% needed phototherapy versus 10.90% in the ECC group. p value = 0.592 which was not statistically significant.

APGAR score at 1 min < 7 was among 59.37% and 54.68% in the ECC group respectively. p value = 0.592. This difference was not statistically significant. The rate of NICU admissions in the DCC group and ECC group was the same, 23.4% (p value = 1). There was no difference in the pregnancy outcome in terms of neonatal mortality rate in the two groups (p = 1).

These findings were consistent with several other studies.

In the study by Kugelman et al, although the bilirubin levels for the total cohort and for the vaginally delivered neonates tended to be higher for the DCC group, the time to start phototherapy and the length of phototherapy were comparable between the ICC and DCC groups. In the subgroup of very low birth weight neonates, there was no difference between the ICC and DCC groups in bilirubin levels. No

neonate needed partial exchange transfusion for polycythemia or total exchange transfusion for hyperbilirubinemia throughout the study.[23]

In the study by Strauss et al, although more neonates needed phototherapy (p = 0.03) after DCC, but initial bilirubin levels and extent of phototherapy did not differ. There were no adverse effects of clinical importance apparent in our neonates 30 to 36 weeks gestation after delayed umbilical cord clamping of 1-minute duration. Although mean Hct values were significantly higher after delayed cord clamping than immediate, the highest mean value was 56 percent—well below 65 percent, the value diagnostic for neonatal polycythemia. Moreover, no infant required phlebotomy for symptoms of polycythemia or hyperviscosity.[20]

In the study by J. Kaempf et al, highest measured total bilirubin concentration and use of phototherapy were not significantly different between the two groups. (p = 0.40 and p = 0.26) respectively. It also concluded that preterm infants <1500 grams had higher 1 minute APGAR scores, less need for supplemental oxygen and mask ventilation and thus is safe in singleton premature infants.[15]

In a recent Cochrane Review by Rabe et al in 2012, which conducted a metaanalysis of 15 studies including 738 infants between 24 and 36 weeks gestation demonstrated that delaying cord clamping for at least 30 to 120 seconds in preterm infants decreased the need for red cell transfusion, and intraventricular hemorrhage. However placental transfusion had no effect on the APGAR score at 1, 5 and 10 minutes.[18]

Thus our study concludes that delayed cord clamping up to 45 seconds appears to be a safe and cost effective beneficial tool which significantly improves the hemoglobin levels in late preterm neonates without significant risk of

hyperbilirubinemia, increased risk of phototherapy, without compromising the APGAR score at birth, if teamed with adequate facilities for recognizing signs and symptoms of respiratory distress needing resuscitation and suctioning, and immediate provision of essential new born care. This can be performed during both cesarean and vaginal delivery, with neonates placed at or below the level of introitus. WHO recommends late cord clamping for all births while initiating simultaneous essential newborn care.

RCOG in Feb 2015 in its scientific impact paper No.14 opined that for preterm births the evidence is less clear than for term births, although data from the trials suggest potential benefit by deferred rather than immediate cord clamping. Strategies and equipment for providing initial neonatal care and resuscitation at the woman's bedside with the cord intact should be developed further and evaluated.[74]

Thus this calls for a change of practice to delayed cord clamping in late preterm neonates.

# CONCLUSION

Overall the present study concluded that delaying the cord clamping by 45 seconds in late preterm neonates between 34 weeks to 36 weeks 6 days period of gestation resulted in an increase in neonatal blood volume during both vaginal delivery and cesarean section. This was assessed by the significant rise in mean hemoglobin levels between 12 – 24 hours of life. Mean hemoglobin level in gram% on day one of life of neonates among delayed cord clamping group was 15.66 ± 3.12 versus 14.05 ± 3.07 among early cord clamping group. p value = 0.0039, which is statistically significant.

Despite the significant increase in blood volume, there was no significant difference in the adverse neonatal outcomes including serum bilirubin levels (total and direct) among the two groups. The total mean serum bilirubin (mg/dL) among delayed and early cord clamping group was 7.92 ± 3.61 and 8.03 ± 3.18 respectively. p value = 0.8552, which is not statistically significant. The mean direct serum bilirubin (mg/dL) was marginally higher in delayed versus early cord clamping group 0.40 ± 0.198 versus 0.371 ± 0.229 respectively. However this difference was not statistically significant p value = 0.449.

There was a slightly increased need of phototherapy for hyperbilirubinemia noted in the delayed cord clamping group compared to early cord clamping group. 14.10% in DCC group versus 10.90% in the ECC group. p value = 0.592 which was not statistically significant

There was no significant difference in the APGAR score between the two groups. APGAR score at 1 min < 7 was 59.37% among DCC versus 54.68% in the

ECC group. p value = 0.59. The rate of NICU admissions (23.4%) and pregnancy outcome in terms of neonatal mortality rate was same in the two groups (p = 1)

Thus delayed cord clamping up to 45 seconds appears to be a safe and cost effective beneficial tool which significantly improves the hemoglobin levels in late preterm neonates without significant risk of hyperbilirubinemia, increased need of phototherapy for hyperbilirubinemia and without compromising the APGAR score at birth. This can be performed during both cesarean and vaginal delivery, with neonates placed at or below the level of introitus.

Hence delayed cord clamping by 45 seconds can be routinely employed in all late preterm neonates delivery vaginally or by cesarean section if teamed with adequate facilities for recognizing signs and symptoms of respiratory distress, with provision for immediate resuscitation and essential new born care.

There is a need for a larger multicentric randomised control trial with a longer period of follow up to reassert the findings of the present study. Studies need to be carried out mainly focussing on cesarean section as most high risk preterm are delivered by cesarean section.

# SUMMARY

The present study was designed to determine whether delayed cord clamping in late preterm neonates between 34 to 36 weeks 6 days period of gestation would result in a better hemoglobin values at birth without increasing the adverse effects and thus improve neonatal outcome during both vaginal and cesarean delivery.

This one year randomized controlled trial was conducted in the Department of Obstetrics and Gynecology, KLE University's Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi during the period of May 2014 to May 2015. A total of 128 pregnant women delivering late premature neonates both vaginally and cesarean sections fulfilling inclusion criteria were included in the study. Based on the computer generated randomization chart, these women were randomized into 2 groups with 64 cases in each arm. In delayed cord clamping group, cord was cut after 45 seconds and in early cord clamping group, cord was clamped within 5 seconds. Babies delivered vaginally were placed just below the level of the introitus and during caesarean deliveries; babies were placed on sterile drapes between the mother's legs. All babies were gently dried, stimulated, suctioning done if needed.

The outcomes assessed were Hb in gm% on Day one of life, highest total serum bilirubin level attained before discharge in mg/dl, APGAR score at 1 and 5 minutes, NICU admission rates, need of phototherapy for hyperbilirubinemia and neonatal mortality rate.

Overall in the present study, mean hemoglobin levels in gram % on day one of life were significantly higher among DCC 15.66 ± 3.12 versus 14.05 ± 3.07 in ECC. p = 0.0039. There was no significant difference in mean total serum bilirubin and

mean direct serum bilirubin in (mg/dl) among DCC and ECC (7.92 ± 3.61 versus 8.03 ± 3.18 p = 0.8552) and (0.40 ± 0.198 versus 0.371 ± 0.229 p = 0.449) respectively. No significant difference was noted in the need for phototherapy (14.10% versus 10.90% p = 0.592) and APGAR score at 1 min < 7 (59.37% versus 54.68%, p = 0.592). Rate of NICU admissions (23.4%) and pregnancy outcome (live birth rates) was same in both groups (p = 1).

Delayed cord clamping by 45 seconds in late preterm neonates can be incorporated in routine practice as it leads to significant increase in hemoglobin levels at birth without increase in adverse neonatal outcomes during both vaginal delivery and cesarean section, thus leading to improvement in neonatal outcome in preterm neonates.

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# ANNEXURE I - ETHICAL CLEARENCE LETTER

K.L.E.SOCIETY'S
**JAWAHARLAL NEHRU MEDICAL COLLEGE,**
**NEHRU NAGAR, BELGAUM-590010 (KARNATAKA-INDIA)**
**(Affiliated to KLE University, Belgaum)**

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**Ref: MDC/DOME/ 101** **Date: 05/12/2013**

To,

PG student in MD. Pulmonary Medicine,
J.N.Medical College,
BELGAUM.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"RELIABILITY AND VALIDITY OF THE CLINICAL COPD QUESTIONNAIRE AND CHRONIC RESPIRATORY QUESTIONNAIRE IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASES TAKING TIOTROPIUM OVER A PERIOD OF 26 WEEKS- A PROSPECTIVE STUDY"**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

**(Dr.Hema Dhumale)**
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belgaum.

**(Dr.Ganga Pilli)**
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belgaum.

# ANNEXURE II – CONSENT FORM

**INFORMED CONSENT FORM FOR PARTICIPATION IN THE RESEARCH STUDY**

Mr/Mrs/Miss. _____ we are requesting you to enrol yourself in study titled **"COMPARISON OF THE OUTCOME OF DELAYED VERSUS EARLY CLAMPING OF THE UMBILICAL CORD IN PREMATURE NEONATES : A RANDOMISED CONTROLLED TRIAL" IN KLE'S DR. PRABHAKAR KORE CHARITABLE HOSPITAL, BELAGAVI-590010",** conducted by Dr. _____, Post Graduate in M.S. OBSTETRICS AND GYNAECOLOGY under the guidance of Dr. _____ Professor, Department of OBSTETRICS AND GYNAECOLOGY, J.N. Medical College, Belgaum under KLE university, Belagavi.

Respected Sir/Madam We request you to enrol yourself to participate in our study as you are eligible for participating in the study. During the study you will be asked some questions regarding your present complaint and you are supposed to answer to the best of your knowledge.

Your participation in this research is voluntary. Your decision whether or not to participate in the study will not affect your relationship with J.N.Medical College. If you decide to participate you are free to withdraw at any time.

**Purpose of the study:**

This study will help to gather evidence that delayed cord clamping will result in better haematocrit and blood volume in the premature and thus better outcome.

**Procedure Involved:**

If you agree to enrol yourself in my study, you will be allotted into one of the two groups randomly using a computer generated software. One group will have delayed cord clamping after 45 seconds and other will have early cord clamping in 5 seconds.

**Risks:**

There is no risk involved in delayed cord clamping according to recent studies.

**Benefits**:

It is an effective and safe procedure to provide better haematocrit and blood volumes and ensure better premature neonate outcome.

**Voluntary Participation/Withdrawal:**

Taking part in the study is voluntary. You may choose not to enrol yourself in this study. Your decision will not change present or future health care services offered to you at K.L.E. hospital.

**Alternatives:**

Even if you decline the participation in the study, you will get the routine line of management.

**Privacy and Confidentiality:**

The only people to know that you are a research subject are members of the research team. No information about you or information provided by you during the research will be disclosed to other without your written permission except:

1. In emergency to protect your rights and welfare.
2. If required by law.

**Authorization to Publish Results:**

When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with your identity remaining confidential.

**Financial Incentives for participation:**

No financial incentives are being offered to enrolled patients. It is purely being done with the idea of research and all the cost of the study will be borne by the investigator.

**Compensation:**

In the event of any untoward complication related to the study, treatment will be made available through KLES' Hospital &MRC, Belagavi. There is no compensation or payment for such medical treatment by law. If untoward complications occur, you may contact Dr. _____, at Department of obstetrics and gynaecology, KLES Hospital & MRC or by Ph. No: _____.

**Questions:**

In case you have any questions related to the study, in future or in case of study related complications or illness, you can contact Dr. _____, Department of obstetrics and gynaecology, KLES Hospital and MRC, Belagavi, phone number: _____, Or Dr. _____, Professor, Dept. Of obstetrics and gynaecology, KLES Hospital and MRC, Belagavi phone number:_____.

If you have any queries about your rights as a study subject, you may call Dr. Ganga Pilli, Professor, Department of Pathology and Chairman, J.N. Medical College Institutional Ethical Committee for Human Subjects Research, Phone number-9448863866, or extension 4052 at J.N. Medical College, Belagavi.

**Consent for participation in research trial**

I, Mr/Ms/Mrs _____ voluntarily agree for the participation as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read for me in vernacular language, including the risks and the benefits and having all my questions answered.

Subject Name : _____

Signature or the Left Thumb Print of Subject : _____

Date:

Witness Name : _____ Signature: _____

Date:

Investigators Name: _____ Signature: _____

Date:

Place : _____

# ಸಂಶೋಧನಾ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪಿಗೆ ಪತ್ರ

ಶ್ರೀ/ಶ್ರೀಮತಿ/ಕುಮಾರಿ_____

ಪ್ರಸೂತಿ ಮತ್ತು ಸ್ತ್ರೀರೋಗ ಶಾಸ್ತ್ರದಲ್ಲಿ ಸ್ನಾತಕೋತ್ತರ ವ್ಯಾಸಂಗ ಮಾಡುತ್ತಿರುವ ಡಾ॥ ಇವರು ಡಾ॥ ಪ್ರಾಧ್ಯಾಪಕರು, ಪ್ರಸೂತಿ ಮತ್ತು ಸ್ತ್ರೀ ರೋಗ ಶಾಸ್ತ್ರ, ಕೆ.ಎಲ್.ಇ. ವಿಶ್ವವಿದ್ಯಾಲಯದ ಜೆ.ಎನ್. ವೈದ್ಯಕೀಯ ಮಹಾವಿದ್ಯಾಲಯ ಅವರ ಮಾರ್ಗದರ್ಶನದಲ್ಲಿ ಮಾಡಿರುವ **"ಅವಧಿ ಪೂರ್ವ ಜನಿಸಿದ ನವಜಾತ ಶಿಶುಗಳಲ್ಲಿ ಹೊಕ್ಕಳ ಬಳ್ಳಿಯನ್ನು ತಡವಾಗಿ ನಿರ್ಬಂಧಿಸುವುದು/ಕ್ಲ್ಯಾಂಪಿಂಗ್** (delayed clamping) **ಮತ್ತು ಬೇಗನೇ ನಿರ್ಬಂಧಿಸುವುದು/ಕ್ಲ್ಯಾಂಪಿಂಗ್** (early clamping) **ಮಾಡುವುದರ ಬಗ್ಗೆ ಅನಿರ್ದಿಷ್ಟವಾಗಿ ಆಯ್ದ ಮಾದರಿಗಳ ಮೇಲೆ ಮಾಡಿದ ನಿಯಂತ್ರಿತ ಪ್ರಯೋಗದ ಒಂದು ತುಲನಾತ್ಮಕ ಅಧ್ಯಯನ"** (Comparison of Delayed Versus Early Clamping of the Umbilical Cord in Premature Neonates, a Radomized Controlled Trial) ದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಆಮಂತ್ರಿಸುತ್ತಿದ್ದೇವೆ.

ನೀವು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಅರ್ಹರಾಗಿರುವುದರಿಂದ ನಿಮ್ಮ ಹೆಸರನ್ನು ನೊಂದಾಯಿಸಲು ನಿಮ್ಮನ್ನು ವಿನಂತಿಸುತ್ತೇವೆ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಸದ್ಯ ನೀವು ಅನುಭವಿಸತ್ತಿರುವ ತೊಂದರೆಗಳ ಬಗ್ಗೆ ಕೆಲವು ಪ್ರಶ್ನೆಗಳನ್ನು ಕೇಳಲಾಗುವುದು. ಅವುಗಳಿಗೆ ನೀವು ನಿಮ್ಮ ಗೊತ್ತಿರುವ ಮಾಹಿತಿಯ ಮೇರೆಗೆ ಉತ್ತರಿಸಬಹುದು.

ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಭಾಗವಹಿಸುವುದು ವೈಯಕ್ತಿಕವಾಗಿದ್ದು, ನೀವು ಇದರಲ್ಲಿ ಭಾಗವಹಿಸಿದರೂ ಅಥವಾ ಭಾಗವಹಿಸದಿದ್ದರೂ ಜೆ.ಎನ್. ವೈದ್ಯಕೀಯ ಮಹಾವಿದ್ಯಾಲಯದ ಜೊತೆಗಿರುವ ನಿಮ್ಮ ಸಂಬಂಧ ಮೇಲೆ ಯಾವುದೇ ಪರಿಣಾಮ ಉಂಟಾಗುವುದಿಲ್ಲ. ನೀವು ಭಾಗವಹಿಸಲು ಇಚ್ಛಿಸಿದರೂ ಸಹ, ನೀವು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಇದರಿಂದ ಹೊರಹೋಗಬಹುದು.

ಈ ಸಂಶೋಧನೆಯ ಮುಖ್ಯ ಉದ್ದೇಶ:

"ಅವಧಿ ಪೂರ್ವ ಜನಿಸಿದ ನವಜಾತ ಶಿಶುಗಳಲ್ಲಿ ಹೊಕ್ಕಳ ಬಳ್ಳಿಯನ್ನು ತಡವಾಗಿ ನಿರ್ಬಂಧಿಸುವುದು/ಕ್ಲ್ಯಾಂಪಿಂಗ್ (delayed clamping) ಮತ್ತು ಬೇಗನೇ ನಿರ್ಬಂಧಿಸುವುದು/ ಕ್ಲ್ಯಾಂಪಿಂಗ್ (early clamping) ಮಾಡುವುದರಿಂದ ಆಗುವ ಪರಿಣಾಮಗಳನ್ನು ಕಂಡು ಹಿಡಿಯುವುದು ಈ ಅಧ್ಯಯನದ ಮುಖ್ಯ ಉದ್ದೇಶವಾಗಿರುತ್ತದೆ.

ಈ ಅಧ್ಯಯನದಿಂದ, ಅವಧಿ ಪೂರ್ವ ಜನಿಸಿದ ನವಜಾತ ಶಿಶುಗಳಲ್ಲಿ ಹೊಕ್ಕಳ ಬಳ್ಳಿಯನ್ನು ತಡವಾಗಿ ನಿರ್ಬಂಧಿಸುವುದು/ಕ್ಲ್ಯಾಂಪಿಂಗ್ ಮಾಡುವುದರಿಂದ ರಕ್ತವೃದ್ಧಿ ಮತ್ತು ರಕ್ತದಲ್ಲಿಯ ಕೆಂಪುಕಣಗಳ ವೃದ್ಧಿಗೊಳ್ಳುವಿಕೆ ಕಂಡು ಬರುತ್ತದೆ ಮತ್ತು ಇದರಿಂದ ಉತ್ತಮ ಪರಿಣಾಮವಾಗುವುದು ಎಂದು ಕಂಡುಬರುತ್ತದೆ.

ಅಧ್ಯಯನವು ಒಳಗೊಂಡಿರುವ ವಿಧಾನ:

ನೀವು ಸದರಿ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನಿಮ್ಮ ಹೆಸರನ್ನು ನೊಂದಾಯಿಸಲು ಒಪ್ಪಿಕೊಂಡರೆ, ಗಣಕೀಕೃತ ತತ್ರಾಂಶವನ್ನು ಬಳಸಿ ನಿಮ್ಮ ಹೆಸರನ್ನು ಎರಡು ಗುಂಪುಗಳಲ್ಲಿ ಯಾವುದೋ ಒಂದು ಗುಂಪಿಗೆ ಸೇರಿಸಲಾಗುವುದು. ಒಂದು ಗುಂಪಿನವರ ಹೊಕ್ಕಳ ಬಳ್ಳಿಯನ್ನು ಮಗು ಜನಿಸಿದ 45 ಸೆಕೆಂಡಗಳ ನಂತರ ಕ್ಲ್ಯಾಂಪಿಂಗ್ ಮಾಡಲಾಗುವುದು ಮತ್ತು ಇನ್ನೊಂದು ಗುಂಪಿನವರಿಗೆ 5 ಸೆಕೆಂಡಗಳ ನಂತರ ಕ್ಲ್ಯಾಂಪಿಂಗ್ ಮಾಡಲಾಗುವುದು.

ಅಪಾಯಗಳು:

ಅವಧಿ ಪೂರ್ವ ಜನಿಸಿದ ನವಜಾತ ಶಿಶುಗಳಲ್ಲಿ ಹೊಕ್ಕಳ ಬಳ್ಳಿಯನ್ನು ತಡವಾಗಿ ನಿರ್ಬಂಧಿಸುವುದು/ಕ್ಲ್ಯಾಂಪಿಂಗ್ ಮಾಡುವುದರಿಂದ ಯಾವುದೇ ಹಾನಿ ಉಂಟಾಗುವುದಿಲ್ಲ ಎಂದು ಇತ್ತೀಚಿನ ಅಧ್ಯಯನಗಳಿಂದ ಕಂಡುಬಂದಿದೆ.

ಪ್ರಯೋಜನಗಳು:

ದೇಹದಲ್ಲಿಯ ರಕ್ತವೃದ್ಧಿ ಮತ್ತು ರಕ್ತದಲ್ಲಿಯ ಕೆಂಪುಕಣಗಳ ವೃದ್ಧಿಗೊಳ್ಳುವಿಕೆಯ ಸಲುವಾಗಿ ಅವಧಿ ಪೂರ್ವ ಜನಿಸಿದ ನವಜಾತ ಶಿಶುಗಳಲ್ಲಿ ಹೊಕ್ಕಳ ಬಳ್ಳಿಯನ್ನು ತಡವಾಗಿ ನಿರ್ಬಂಧಿಸುವುದು/ಕ್ಲ್ಯಾಂಪಿಂಗ್ ಮಾಡುವುದು ಒಂದು ಪರಿಣಾಮಕಾರಿಯಾದ ಮತ್ತು ಸುರಕ್ಷಿತ ವಿಧಾನವಾಗಿದೆ.

**ಸ್ವಯಂ ಪ್ರೇರಿತ ಭಾಗವಹಿಸುವಿಕೆ/ಹೊರ ಹೋಗುವುದು:**

ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವುದು ಸಂಪೂರ್ಣ ವೈಯಕ್ತಿಕವಾಗಿರುತ್ತದೆ. ನೀವು ಇದರಲ್ಲಿ ಭಾಗವಹಿಸಲು ನಿಮ್ಮ ಹೆಸರನ್ನು ನೊಂದಾಯಿಸದಿದ್ದರೂ ಸಹ ನೀವು ಇದರಲ್ಲಿ ಭಾಗವಹಿಸಿದರೂ ಅಥವಾ ಭಾಗವಹಿಸದಿದ್ದರೂ ಕೆ.ಎಲ್.ಇ.ಎಸ್. ಆಸ್ಪತ್ರೆಯ ಜೊತೆಗಿರುವ ನಿಮ್ಮ ಸಂಬಂಧ ಮೇಲೆ ಯಾವುದೇ ಪರಿಣಾಮ ಉಂಟಾಗುವುದಿಲ್ಲ.

**ಪರ್ಯಾಯ/ಬದಲಿ:**

ನೀವು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸದಿದ್ದರೂ, ನಮ್ಮ ದಿನ ನಿತ್ಯದ ನಿರ್ವಹಣೆಯಲ್ಲಿ ಯಾವುದೇ ವ್ಯತ್ಯಾಸವಾಗುವುದಿಲ್ಲ.

**ಗೌಪ್ಯತೆಯ ರಕ್ಷಣೆ:**

ನಿಮ್ಮ ಬಗೆಗಿನ ವಿವರಗಳು ಸಂಶೋಧನಾ ತಂಡದವರಿಗೆ ಮಾತ್ರ ತಿಳಿದಿರುತ್ತದೆ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನೀವು ಒದಗಿಸುವ ಯಾವುದೇ ಮಾಹಿತಿಯನ್ನು (ಈ ಕೆಳಗಿನ ಸಂದರ್ಭಗಳನ್ನು ಬಿಟ್ಟು) ನಿಮ್ಮ ಲಿಖಿತ ಪರವಾನಿಗೆ ಇಲ್ಲದೇ ಬೇರೆಯವರಿಗೆ ಕೊಡಲಾಗುವುದಿಲ್ಲ.

1) ನಿಮ್ಮ ಹಕ್ಕು ಮತ್ತು ಹಿತರಕ್ಷಣೆ ಸಲುವಾಗಿ ತುರ್ತು ಸಂದರ್ಭಗಳಲ್ಲಿ
2) ಕಾನೂನಿನ ಪ್ರಕಾರ ಯಾವುದೇ ಮಾಹಿತಿ ಒದಗಿಸಬೇಕಾದ ಸಂದರ್ಭದಲ್ಲಿ

**ಅಧ್ಯಯನದ ಫಲಿತಾಂಶಗಳನ್ನು ಪ್ರಕಟಿಸುವ ಅಧಿಕಾರ:**

ಈ ಸಂಶೋಧನೆಯ ಫಲಿತಾಂಶಗಳನ್ನು ಪ್ರಕಟಿಸಿದಾಗ ಅಥವಾ ಚರ್ಚಿಸುವಾಗ ನಿಮ್ಮ ಯಾವುದೇ ವೈಯಕ್ತಿಕ ಗುರುತನ್ನು ಬಹಿರಂಗಪಡಿಸುವ ಯಾವುದೇ ಮಾಹಿತಿಯನ್ನು ಕೊಡಲಾಗುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಯಾವುದೇ ಮಾಹಿತಿಯನ್ನು ಗೌಪ್ಯವಾಗಿಡಲಾಗುವುದು.

**ಭಾಗವಹಿಸುವುದರಿಂದ ಆರ್ಥಿಕ ಪ್ರೋತ್ಸಾಹಗಳು:**

ನೀವು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನಿಮ್ಮ ಹೆಸರನ್ನು ನೊಂದಾಯಿಸಿದರೆ ನಿಮಗೆ ಯಾವುದೇ ಆರ್ಥಿಕ ಪ್ರೋತ್ಸಾಹಗಳನ್ನು ಕೊಡಲಾಗುವುದಿಲ್ಲ. ಇದನ್ನು ಕೇವಲ ಸಂಶೋಧನೆಗಾಗಿ ಮಾಡಲಾಗುವುದು ಮತ್ತು ಇದರ ಎಲ್ಲ ಖರ್ಚುವೆಚ್ಚಗಳನ್ನು ಸಂಶೋಧಕರೇ ಭರಿಸುತ್ತಾರೆ.

<u>ಪರಿಹಾರ:</u>

ಈ ಅಧ್ಯಯನಕ್ಕೆ ಸಂಬಂಧಪಟ್ಟಂತೆ ನಿಮಗೆ ಯಾವುದೇ ಗಾಯಗಳಾದರೆ, ಕೆ.ಎಲ್.ಇ.ಎಸ್. ಆಸ್ಪತ್ರೆ ಮತ್ತು ಎಮ್.ಆರ್.ಸಿ. ವತಿಯಿಂದ ಚಿಕಿತ್ಸೆ ನೀಡಲಾಗುವುದು. ಈ ರೀತಿಯ ವೈದ್ಯಕೀಯ ಚಿಕಿತ್ಸೆಗೆ ಯಾವುದೇ ಪರಿಹಾರಧನ ಕೊಡಲಾಗುವುದಿಲ್ಲ. ನಿಮಗೆ ಯಾವುದೇ ಗಾಯವಾದ ಸಂದರ್ಭದಲ್ಲಿ ನೀವು ಡಾ॥ ಪ್ರಸೂತಿ ಮತ್ತು ಸ್ತ್ರೀರೋಗ ಶಾಸ್ತ್ರ ವಿಭಾಗ, ಕೆ.ಎಲ್.ಇ.ಎಸ್. ಆಸ್ಪತ್ರೆ ಮತ್ತು ಎಮ್.ಆರ್.ಸಿ. ಇವರನ್ನು ಅಥವಾ ಮೊಬೈಲ ನಂ. ಮೂಲಕ ಸಂಪರ್ಕಿಸಬಹುದು.

<u>ಪ್ರಶ್ನೆಗಳು:</u>

ಈ ಅಧ್ಯಯನಕ್ಕೆ ಸಂಬಂಧಿಸಿದಂತೆ ನೀವು ಯಾವುದೇ ಪ್ರಶ್ನೆಗಳನ್ನು ಕೇಳಬೇಕಾಗಿದ್ದರೆ, ನೀವು ಡಾ॥ ಸಮೀರ ಕುಲಕರ್ಣಿ, ಪ್ರಸೂತಿ ಮತ್ತು ಸ್ತ್ರೀರೋಗ ಶಾಸ್ತ್ರ ವಿಭಾಗ, ಕೆ.ಎಲ್.ಇ.ಎಸ್. ಆಸ್ಪತ್ರೆ ಮತ್ತು ಎಮ್.ಆರ್.ಸಿ., ಫೋನ್: 8861353066 ಅಥವಾ ಡಾ॥ ಪ್ರಾಧ್ಯಾಪಕರು, ಸ್ತ್ರೀರೋಗ ಶಾಸ್ತ್ರ ವಿಭಾಗ, ಕೆ.ಎಲ್.ಇ.ಎಸ್. ಆಸ್ಪತ್ರೆ ಮತ್ತು ಎಮ್.ಆರ್.ಸಿ. ಫೋನ: । ಇವರನ್ನು ಸಂಪರ್ಕಿಸಬಹುದು,

ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಪ್ರಯೋಗಾರ್ಥಿಯಾಗಿ ನಿಮ್ಮ ಹಕ್ಕುಗಳ ಬಗ್ಗೆ ಯಾವುದೇ ಪ್ರಶ್ನೆಗಳಿದ್ದರೆ, ನೀವು ಡಾ॥ ಗಂಗಾ ಪಿಳ್ಳೈ, ಪ್ರಾಧ್ಯಾಪಕರು ಮತ್ತು ಪೆಥಾಲಾಜಿ ವಿಭಾಗದ ಮುಖ್ಯಸ್ಥರು, ಚೇರಮನ್ ಜೆ.ಎನ್. ಮೆಡಿಕಲ್ ಕಾಲೇಜ್ ಇನ್ಸಸ್ಟಿಟ್ಯೂಷನಲ್ ಎಥಿಕ್ಸ್ ಕಮೀಟಿ ಆನ್ ಹ್ಯುಮನ್ ಸಬ್ಜೆಕ್ಟ್ಸ್ ರಿಸರ್ಚ, ಮೊಬೈಲ್ ನಂ.: 9448863866 ಮೂಲಕ ಸಂಪರ್ಕಿಸಬಹುದು.

**"ಅವಧಿ ಪೂರ್ವ ಜನಿಸಿದ ನವಜಾತ ಶಿಶುಗಳಲ್ಲಿ ಹೊಕ್ಕಳ ಬಳ್ಳಿಯನ್ನು ತಡವಾಗಿ ನಿರ್ಬಂಧಿಸುವುದು/ಕ್ಲ್ಯಾಂಪಿಂಗ್** (delayed clamping) **ಮತ್ತು ಬೇಗನೇ ನಿರ್ಬಂಧಿಸುವುದು/ ಕ್ಲ್ಯಾಂಪಿಂಗ್** (early clamping) **ಮಾಡುವುದರ ಬಗ್ಗೆ ಅನಿರ್ದಿಷ್ಟವಾಗಿ ಆಯ್ದ ಮಾದರಿಗಳ ಮೇಲೆ ಮಾಡಿದ ನಿಯಂತ್ರಿತ ಪ್ರಯೋಗದ ಒಂದು ತುಲನಾತ್ಮಕ ಅಧ್ಯಯನ" ವನ್ನು ಡಾ॥ ಪ್ರಭಾಕರ ಕೋರೆ ಆಸ್ಪತ್ರೆ, ಬೆಳಗಾವಿ – ೮೨೦೦೧೦ ದಲ್ಲಿ ನಡೆಸಲಾಗುವುದು.**

## ಈ ಸಂಶೋಧನಾ ಪ್ರಯೋಗದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪಿಗೆ

ಈ ಕೆಳಗೆ ಸಹಿ ಮಾಡಿದ _____

ಸ್ವಯಂಪ್ರೇರಿತವಾಗಿ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪಿಕೊಂಡಿರುತ್ತೇನೆ. ಈ ಒಪ್ಪಿಗೆ ಪತ್ರಕ್ಕೆ ಸಹಿ ಮಾಡುವುದರಿಂದ ನಾನು ನನ್ನ ಯಾವುದೇ ಕಾಯದೆಬದ್ಧ ಹಕ್ಕುಗಳನ್ನು ಬಿಟ್ಟುಕೊಟ್ಟಿರುವುದಿಲ್ಲ. ನಾನು ಯಾವುದೇ ಸಂದರ್ಭದಲ್ಲಿ ಈ ಅಧ್ಯಯನದಿಂದ ಹೊರಹೋಗಬಹುದು. ನಾನು ಈ ಅಧ್ಯಯನವು ಒಳಗೊಳ್ಳುವ ಅಪಾಯಗಳು ಮತ್ತು ಪ್ರಯೋಜನಗಳು ಹಾಗೂ ಪ್ರಶ್ನೆಗಳಿಗೆ ನಾನು ಕೊಟ್ಟಿರುವ ಉತ್ತರಗಳನ್ನು ನನ್ನ ಮಾತೃಭಾಷೆಯಲ್ಲಿ ಓದಿ, ತಿಳದುಕೊಂಡು ನನ್ನ ಒಪ್ಪಿಗೆಯನ್ನು ಕೊಟ್ಟಿರುತ್ತೇನೆ.

ಪ್ರಯೋಗಾರ್ಥಿಯ ಹೆಸರು : _____

ಪ್ರಯೋಗಾರ್ಥಿಯ ಸಹಿ: _____
ಅಥವಾ ಎಡಗೈ ಹೆಬ್ಬಟ್ಟಿನ ಗುರುತು

ಸಹಿ:_____

ದಿನಾಂಕ: _____

# ANNEXURE III - DATA COLLECTION INSTRUMENT

**TITLE: "COMPARISON OF THE OUTCOME OF DELAYED VERSUS EARLY CLAMPING OF THE UMBILICAL CORD IN PREMATURE NEONATES: A RANDOMISED CONTROLLED TRIAL.**

- IP.NO :
- PATIENT.NO :

## 1. SUBJECT INFORMATION

- NAME :
- AGE :
- ADDRESS :
- OCCUPATION
- RELIGION

## 2. CURRENT PREGNANCY

- GRAVIDA
- PARA :
- LIVING :
- ABORTION :
- LMP :
- EDD :
- PERIOD OF GESTATION :
- ANY COMPLICATIONS IN PRESENT PREGNANCY LIKE PIH, GDM, IUGR, PROLONGED RUPTURE OF MEMBRANES

**3. GENERAL EXAMINATION**

- HEIGHT :
- WEIGHT :
- BMI :
- PALLOR:

**4. VITALS**- PR: BP:

**P/A:**

**5. INFORMATION ON LABOUR**

- DATE AND TIME WHEN LABOUR STARTED:
- DATE AND TIME OF DELIVERY :
- TYPE OF DELIVERY : SPONTANEOUS/ INDUCED
- REASON IF INDUCED :
- WAS THE CASE RANDOMISED? YES=1 NO=2 :

**6. INFORMATION OF THE BABY**

- GESTATIONAL AGE :
- STEROIDS GIVEN? YES=1 NO=2 :
- TIME OF BIRTH :
- SEX :
- WEIGHT IN KGS :
- DID THE BABY CRY AFTER BIRTH :
- DID THE BABY NEED RESUSCITATION? YES=1 NO=2 :
- APGAR SCORE : 1MINUTE : 5MINUTE :
- HAMATOCRIT AT 12 HOURS :

- SERUM BILIRUBIN LEVELS AT 12 HOURS :
- SIGNATURE AND NAME OF THE INVESTIGATOR :

**Observations**

**Readings were recorded in the following manner:**

**Procedure used: _____.**

**Group: _____**

**DEMOGRAPHIC AND DELIVERY ROOM MEASURES**

| Variables | ECC | DCC |
|---|---|---|
| **No of neonate** | | |
| **Gestational age** | | |
| **Weight** | | |
| **Caesarean delivery** | | |
| **Vaginal delivery** | | |
| **APGAR 1minute** | | |
| **APGAR 5minute** | | |
| **Delivery room resuscitation** | | |

**LABORATORY AND CLINICAL MESURES**

| **Variables** | **ECC** | **DCC** |
|---|---|---|
| **Hb in Gm% at 12 - 24hrs** | | |
| **Peak Total Bilirubin attained before discharge in mg/dl** | | |
| **Peak Direct Bilirubin attained before discharge in mg/dl** | | |

**COMPLICATIONS**

| **Complications** | **ECC** | **DCC** |
|---|---|---|
| **NICU admission** | | |
| **Need for phototherapy for hyperbilirubinemia** | | |
| **Mortality** | | |

Signature of staff in charge:

# ANNEXURE IV – KEY TO MASTER CHART

| | |
|---|---|
| P | - Primigravida |
| M | - Multigravida |
| VD | - Vaginal Delivery |
| LSCS | - Lower Segment Cesearn Section |
| P LSCS | – Previous LSCS |
| PPROM | - Preterm Premature Rupture of Membranes |
| SPE | - Severe Pre Eclampsia |
| IUGR | - Intra Uterine Growth Restriction |
| NVBAC | - Not willing for vaginal birth after cesarean section |
| NPL | - Non Progress of Labour |
| FI | - Failed Induction |
| POLY | - Polyhydramnios |
| CPD | - Cephalopelvic Disproportion |
| B | - Breech |
| E | - Eclampsia |
| N M | -Neonatal mortality |
| TSBL | -Total serum bilirubin levels |
| DSBL | -Direct serum bilirubin levels |
| POG | -Period of gestation |